# OPIOID POISONING AND AVAILABILITY OF SPECIALIZED MEDICAL CARE IN ONTARIO, 2002-2006

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**Abstract**

The prescription of opioid analgesics has risen sharply in North America over the past two decades. This increase has been accompanied by a rise in overdoses. The present study draws on administrative data collected from emergency department contacts to describe the epidemiology of opioid overdose in Ontario between 2002 and 2006 and to examine the role of regional variation in availability of specialist care.

The number of poisonings increased from 1250 (10.9 per 100,000) in FY2002 to 1816 (15.2 per 100,000) in FY2005. Local concentration of specialist physicians was significantly associated with the incidence of opioid overdose, inversely at most levels of availability, but positively at very high levels. Regional variation in incidence was also associated with demographics, median family income, and the rate of other drug poisonings. Policy options for limiting opioid-related harms are limited, but improvements in monitoring and clinical management may prove valuable.

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**Opioids: Description and pharmacology**

The opioids comprise a broad class of drugs with effects similar to those of opium and other derivatives of the opium poppy. They include opiates, which are natural alkaloids derived from the plant itself (e.g., codeine, morphine), semi-synthetic drugs produced from these substances (e.g., heroin, oxycodone), and fully synthetic drugs (e.g., methadone, tramadol) (Kalant, 2006). Opioids medications currently widely prescribed in Canada are listed in table 1.

All widely-used opioids are more or less potent analgesics and have a variety of other effects, including sedation, improved mood, and suppression of the cough reflex (Merck 2008; Kalant, 2006; Benyamin et al. 2008). Common undesirable side effects of opioids include constipation, dizziness, nausea, vomiting, paradoxical hypersensitivity to pain, hormonal changes, and respiratory depression. The majority are also capable of producing euphoria, which has led to widespread non-medical use. Opioids are effective because of their similarity to chemicals produced by the body that modulate a number of behavioral drives and biological functions (Akil et al. 1998; Van Ree et al. 2000). These 'endogenous opioids,' including endorphins, enkephalins, dynorphins, and endomorphins, play important roles in respiration, digestive system function, sexual drive, social behaviour, analgesia, and reward.

Medically, opioids are most commonly used for analgesia in cases of moderate or severe pain. They may be prescribed for postsurgical pain or traumatic injury, or to manage chronic conditions such as cancer, lower back pain, neuropathic pain, or

osteoarthritis. Other medical uses, which typically involve low doses or relatively low-potency opioids such as codeine, include the treatment of diarrhea or coughing. While alternatives exist for their other uses, opioids are indispensable for the treatment of pain, for which there are no other drug or non-drug therapies of comparable effectiveness (WHO, 2000). A less widely-appreciated effect of opioids is the reduction of suffering generally, including emotional distress. Physical and emotional pain share common neurochemical bases (e.g., Vastag, 2003), and, in the same way that antidepressants have proven effective against some forms of chronic pain (e.g., Ansari 2000), opioids appear to be effective against depression and anxiety (Jamison et al. 1998; Haythornthwaite et al. 1998). This may be an important component of opioid therapy in palliative care, and may also account for some of their wider use, both medical (Sullivan et al. 2005) and non-medical.

*Table 1. Widely-prescribed opioids.*

| Opioid | Trade names | Approximate relative potency for analgesia (oral dose; morphine = 1) | Doses (all strengths) dispensed at Ontario retail pharmacies, 2005 (millions)*** |
|---|---|---|---|
| Morphine | MS Contin, Oramorph | 1 | 32.2 |
| Codeine | Tylenol 2, 3, 4 | 0.1 | 242.4 |
| Oxycodone | OxyContin, Percocet, Percodan, Tylox | 2 | 43.6 |
| Hydrocodone | Vicodin | 0.5 | 27.0 |
| Hydromorphone | Palladone, Dilaudid, Hydromorph Contin | 4 | 23.6 |
| Methadone | Dolophine | 1.5 | 1.0 |
| Meperidine | Demerol | 0.125 | 4.6 |
| Fentanyl* | Duragesic, Actiq | 150** | 2.9 |

* Limited consensus on equianalgesic dose.
** For transdermal dose.
*** Includes combination preparations.

Sources: Galvagno et al. (2007); Nissen et al. (2001), IMS Health.

The other significant medical use of opioids is in agonist therapy for opioid dependence. Since opioids are cross-tolerant (Kalant, 2006), giving one drug can reduce or eliminate symptoms of withdrawal from another. The prototypical form of opioid agonist therapy is maintenance therapy for heroin dependence, in which people dependent on heroin are given regular doses of another opioid, usually methadone or buprenorphine (First & Tasman, 2006). This ameliorates withdrawal symptoms and reduces cravings for the preferred drug. Methadone and buprenorphine also reduce or eliminate the euphoria and other positive effects felt if use of heroin or another opioid is resumed, and buprenorphine is sometimes given in a formulation that includes the opioid antagonist naloxone, with the intention of preventing intravenous and other unintended use.

**Opioid safety**

Opioids do not cause direct organ damage even with heavy, long-term use, and are generally regarded as remarkably non-toxic (Kalant, 2006). In medical contexts, most practical issues with opioids, apart from misuse and physical dependence, arise from relatively benign side effects. There is, however, some evidence linking opioids to various health problems. Chronic use appears to interfere with immune function, and it has been suggested that this may contribute to the very high prevalence of infectious disease among heroin users (Vallejo et al., 2004). Methadone and the long-acting opioid levo-alpha acetyl methadol (LAAM) – used extensively, until recently, in agonist therapy for opioid dependence (Jaffe, 2007) – have also been shown to

increase risk for heart rhythm abnormalities, including Q-T prolongation and torsades des pointes (Krantz et al., 2003; Krantz et al., 2002). Finally, meperidine (Demerol) has been linked to certain neuropsychiatric side effects, which have led in recent years to substantial reductions in its use (Latta et al., 2002).

A more common concern with opioid use is the potential of all important drugs in this class for misuse. Opioids are both habit-forming and physiologically addictive. Regular use quickly results in tolerance and habituation, and a withdrawal syndrome will occur if use is stopped suddenly or an antagonist drug is used. While not usually medically dangerous, opioid withdrawal is notoriously unpleasant, with symptoms including hypersensitivity to pain, dysphoria, aches, restlessness, sweating, chills, piloerection, irritability, anxiety, weakness, cramps, insomnia, nausea, diarrhea, and hypertension. Induction of sudden, severe opioid withdrawal has been described by those who have experienced it as "the worst feeling in the world" (Worthington et al., 2006).

Cessation of use in non-medical users is also likely to result in strong drug cravings (Kalant, 2006; First & Tasman 2006). Although opioids such as diacetylmorphine (heroin) and morphine have historically been thought to be uniquely appealing to recreational users, most strong opioids appear to be roughly comparable in terms of their potential for misuse. A recent experiment in which several different opioids were administered to morphine-maintained heroin-dependent individuals reported that oxycodone was, in fact, preferred even to heroin (Comer et al. 2008).

**Opioid overdose**

Misuse of opioids is an important factor in their other significant drawback, the risk of overdose. If taken in large quantities, most useful opioids cause suppression of the respiratory centres of the brainstem (White & Irvine, 1999); breathing slows and may eventually cease, leading to death from hypoxia. Associated signs and conditions include pulmonary or cerebral edema, miosis, cyanosis, and coma (Merck manual; Kalant, 2006; White & Irvine 1999). Opioids' emetic and antitussive effects can present a further danger from aspiration of vomit (Henry, 1994).

Death from opioid poisoning is usually slow. Several studies (reviewed in Warner-Smith, 2001) have shown that a large proportion of fatal heroin overdoses occur over a period of hours. In the case of methadone, which has an exceptionally long half-life and accumulates over time, signs of overdose may be apparent days, and are usually visible for hours, before death (Caplehorn 1998). Treatment for overdose is very effective if medical attention is sought promptly; the opioid antagonist naloxone can rapidly reverse an overdose, albeit sometimes at the cost of precipitating instant withdrawal. If necessary, mechanical ventilation can be also used to maintain oxygenation (Greene et al., 2005).

Opioid overdose typically occurs when one or more of four risk factors are present: resumption of use after a period of abstinence or detoxification; use of a substance of unknown purity; use by an individual with health problems that impair hepatic or

pulmonary function; or use in combination with other drugs. The first two of these occur principally among illicit users. The purity of heroin is difficult for users to establish, and may vary considerably over time or between areas. Increases in the purity of available heroin has been shown to be associated with increases in overdose deaths (Darke, 1999). In the context of misuse of prescription opioids, a possibly analogous problem is confusion over or misrepresentation of the active drug or dose thereof.

An issue more germane to the present study is that users, both licit and illicit, often fail to appreciate the dangers posed by changes in tolerance (Gitlow 2002), which is quickly eroded by abstinence. If a former user takes his or her typical dose after a period of non-use, the risk of overdose becomes extreme. The incidence of fatal overdose among heroin users recently released from prison – where limited access to narcotics usually means a period of enforced abstinence – is particularly high (Seamean 1998). This problem has also been frequently noted, however, in the context of drug treatment, particularly following courses of treatment with the opioid antagonist naltrexone (Gibson & Degenhardt, 2007). Although the vast majority of the extant literature deals with heroin overdose, these two factors may also play a role among users of prescription drugs. Patients or users who stop and then resume use of opioid medications may experience overdose as the result of lost tolerance, and this outcome may also occur as the result of confusion over dosages or drug names (particularly when these drugs are used non-medically).

The other significant risk factor, combination of opioids with other drugs, is the norm rather than the exception in fatal opioid overdoses among both medical and illicit users. A number of studies have reported that other substances are found at autopsy in the majority of deaths attributed to heroin overdose (Darke & Zador, 1994; Coffin et al., 2003), while a recent American study found that other potentially contributing substances were present in 97% of deaths involving oxycodone between 1999 and 2002 (Cone et al., 2003). A review of hydromorphone fatalities in Ontario similarly found that alcohol or other drugs were present in the majority of cases (Wallage & Palmentier 2006).

The substances that most commonly play a role in deaths from opioid poisoning are other widely-used respiratory depressants. Benzodiazepines such as diazepam (Valium), lorazepam (Ativan), and alprazolam (Xanax) are particularly prominent in fatal overdoses (White & Irvine 1998). Although other medications such as barbiturates have similar or greater potential to cause respiratory depression, they are now much less widely prescribed than the benzodiazepines (Lader, 1991). Since alcohol is by far the most widely-used intoxicating drug in North America and has independent respiratory depressant effects, it too often plays a role in opioid overdose. The release of some sustained-release prescription opioids may also be accelerated by alcohol. This has been shown to be the case for hydromorphone preparations, which has led Health Canada to recommend that patients be cautioned against this combination (Murray & Wooltorton 2005).

Roles for alcohol and benzodiazepines are supported by forensic and other evidence. Blood alcohol levels and blood opioid levels have been shown to be negatively correlated among victims of fatal overdose, which indicates that alcohol appears to lower the lethality threshold for opioid poisoning (Zador et al., 1996). Similarly, a recent review of fatal heroin overdoses in the United Kingdom found that evidence of recent benzodiazepine use was significantly more common in these cases, at 48%, than among people presenting for treatment of heroin dependence (26%) (Oliver et al., 2007). Use of benzodiazepines and related drugs is also common among people with physical health problems (Neutel, 2005), and issues surrounding their prescription are similar to those associated with the use of opioids.

There is also some evidence that pre-existing health problems can heighten the risk of opioid overdose. It has been suggested that poor liver functioning, in particular, is a common and important risk factor (Warner-Smith 2001; Darke 2006). Since opioids are metabolized in the liver, reduced clearance in people with impaired hepatic function may result in a lengthened period of respiratory depression. It has been argued that hepatitis C, which is highly prevalent among injection drug users, may play a role in some heroin poisonings through its effects on liver functioning (Warner-Smith 2001). A further possibility relevant to prescription opioids concerns acetaminophen, which is hepatotoxic in large doses (Routledge et al., 1998) and which is combined with opioid analgesics in many preparations. Use of large quantities of acetaminophen-containing medications (e.g., Tylenol 1, Tylenol 3, Percocet) may result in impaired liver function, which could increase susceptibility to

opioid poisoning. Alternatively, overdose on a medication containing acetaminophen may lead to simultaneous opioid and acetaminophen poisoning, or to primary acetaminophen poisoning complicated by opioid intoxication. Reduced pulmonary function as the result of smoking, either of tobacco or of other drugs, may also exacerbate the effects of slowed respiration after a large dose of opioids (Warner-Smith 2001). Since liver and lung functioning may also be more commonly impaired among both legitimate medical users and illicit users of opioids, these considerations may also be relevant to overdose from prescription drugs.

Although other factors are usual in poisonings, opioids may also be dangerous or fatal on their own if taken in excessive amounts. In the context of medical use, opioid-only overdoses have occurred as the result of misunderstandings about appropriate use, consumption of more than the prescribed dose, or other unfortunate circumstances. Overdoses of the highly potent opioid fentanyl, for example, have occurred from the use of heating blankets with transdermal patches, which accelerates the release of medication (Frölich et al. 1998; Carter 2003).

**Epidemiology of opioid use**

The vast majority of opioids are used in developed countries. Their use has increased considerably in recent years, approximately doubling (in terms of morphine equivalents) between 2002 and 2007. Increases have been particularly steep for the synthetic and semi-synthetic opioids (International Narcotics Control Board, 2007).

Levels of opioid consumption in Canada, while somewhat below those in the United States, are among the highest in the world; on a per capita basis, Canada is second only to the United States in consumption of oxycodone and is the number one consumer of hydromorphone. In 2006, Canada, with approximately 0.5% of the world's population, consumed 28% of the total global supply of hydromorphone (International Narcotics Control Board, 2007). Over 107 million doses of strong opioids, principally oxycodone, morphine, and hydromorphone, were dispensed from Ontario retail pharmacies in 2005 (IMS Health; table 1). This increased to 121 million in 2006 and to 133 million in 2007. There are limited data on the numbers of users these sales data represent. Among Ontario respondents to cycle 1.1 of the Canadian Community Health Survey, however, approximately 6% reported past-month use of "codeine, Demerol, or morphine" (unpublished data).

Increased use of opioids over the past 10 or 15 years has been driven largely by increased prescription of opioids for pain management, although use of methadone in addiction treatment programs also rose over this period. Increases in opioid prescribing in North America coincided with the introduction and marketing of extended-release formulations such as OxyContin. Medications in these forms were initially believed to have limited potential for recreational use. This may have been a factor in the increase in physicians' willingness to prescribe strong opioids, and was certainly a cornerstone of some companies' marketing efforts (GAO, 2003; Van Zee, 2009). These formulations do, however, retain the potential for recreational use, and

the sustained release features are trivially easy to bypass: Crushing or chewing tablets will cause the drugs they contain to be rapidly released.

**Epidemiology of opioid misuse**

In 1993, a report from the U.S. National Institute on Drug Abuse reviewed existing epidemiological evidence on prescription medication misuse generally and concluded that "the vast majority of prescribed use of these drugs is conservative, therapeutically appropriate, and limited to short periods of time". It went on to note that more than 95% of users reported having been prescribed the drugs they used, and that "consumer attitudes toward taking psychoactive prescription drugs are also conservative" (NIDA, 1993).

During the 1990s, significant changes occurred in prescriptions of opioids and, arguably, in popular attitudes towards the use of analgesics and psychotropic medications. Opioid prescriptions, as noted, increased sharply. Although there is some evidence that the increase in opioid prescription in the first half of the 1990s did not immediately result in increased misuse (Joranson et al., 2000), most indicators of non-medical use since that time suggest that it has grown in step with the total availability of opioids (e.g., Dasgupta et al., 2006). Although some initial trials of extended-release opioid formulations suggested their potential for misuse was limited (GAO 2003), it is now clear that this is not the case.

A 2005 study of illicit users of opioids in 7 Canadian cities found that heroin was used by only 30%, and illegally-obtained methadone by only 9%. Instead, prescription drugs accounted for the majority of illicit opioid use, and appeared to be in the process of displacing drugs such as heroin (Fischer et al., 2006). Patterns of use varied substantially between cities, with heroin predominating in Vancouver and Montreal and other opioids in Edmonton and Quebec City. Among study participants from Toronto (n=141), 53% reported past-month heroin use, 42% hydromorphone, 69% codeine, 31% illegally-obtained methadone, and 84% "other opioids" (Fischer et al. 2005). Similarly, in an ongoing study of 546 outpatients in substance abuse treatment in Toronto, Niagara, and Oshawa, 36% (194 of 537 responding) reported past-year use of prescription opioids, while only 7.4% (40 of 535) had used heroin (Rush et al., in preparation).

Recreational use of opioids also appears to have become widespread among Ontario adolescents. 21% of students surveyed in the 2007 Ontario Student Drug Use and Health Survey (OSDUHS) reported past-year non-medical use of a prescription opioid, with use somewhat more common in northern Ontario and less so in Toronto (Adlaf & Paglia-Boak, 2007). In the 2009 survey, this proportion fell slightly, to 18% (Paglia-Boak et al., 2009). 40% of students who did report using prescription opioids in the past year did so on only one or two occasions (unpublished data).

In the recently-released Canadian Youth Smoking Survey (YSS), conducted in 2006 and 2007, 6.1% of all Ontario secondary school students, and 8.5% of those in grade

12, reported ever having "used painkillers to get high" (unpublished data). Although comparable data for Canada are unavailable, treatment episodes for abuse of or dependence on prescription opioids increased 45% in the United States between 1994 and 1999 (CPDD 2003: SAMSHA, 2001, 2002).

Although all use of opioids without both a prescription and an appropriate, diagnosed medical condition is typically considered 'misuse' or 'abuse', recent research has shown that the distinction between medical and recreational users is often difficult to make. A recent study of opioid users in the rural United States reported that many people with legitimate prescriptions for pain also reported recreational use, while many illicit users reported use for analgesia (Havens et al. 2008). Other studies have similarly noted that pain relief is one of the most frequently endorsed motives for the use of non-prescribed opioids (McCabe et al., 2007). Differences between Ontario epidemiological surveys in estimates of opioid "misuse" suggest that this issue is a significant one; the YSS and the OSDUHS both surveyed the population of Ontario secondary school students during the same year, but, as noted, the YSS reported a much lower prevalence. This may be explained, in part, by the fact that the YSS asked about "[use of] painkillers to get high" (YSS 2007), while OSDUHS asked about use of any of several common prescription opioids "without a prescription or without a doctor telling you to take them" (OSDUHS 2009).

Both legitimate and illicit use of prescription opioids are associated with age. Use without prescriptions has been shown in epidemiological studies to be most common

among younger people, particularly those under approximately age 25 (Manchikanti & Singh, 2008). Serious consequences, including overdose, are more commonly seen among men (e.g., Hall et al., 2008) and at somewhat greater ages, with mean ages of 30 or somewhat more typical in studies of overdose fatalities (Hall et al., 2008; Darke, 1996).

**Sources of opioids**

Opioid analgesics may be obtained by legitimate prescription, by forged prescriptions, from internet pharmacies, by prescriptions obtained by misleading physicians, by physicians knowingly prescribing opioids for non-medical use, or by theft from pharmacies or other facilities (Health Canada, 2006). Significant quantities are stolen. A recent study using data from 22 eastern American states, representing roughly half the national population, found that 1.8 million doses of strong opioids (fentanyl, hydromorphone, meperidine, methadone, morphine, and oxycodone) and 4 million doses of hydrocodone were reported stolen in 2003. 89% of these thefts were from pharmacies (Joranson & Gilson 2005).

Most opioids used non-medically are ultimately obtained from physician prescriptions, however, either directly (by "doctor shopping" or by feigning or exaggerating physical health problems; Zacny et al. 2003) or from other individuals who give away or sell their medications. There is some evidence that the latter pattern is predominant: A report on prescription opioid-related fatalities in West Virginia noted that only 44% of decedents had been prescribed the medication that

killed them, and only 29% had filled such a prescription in the previous 30 days, despite the fact that this is the maximum supply of schedule II drugs that may be dispensed in West Virginia (Hall et al., 2008). Most respondents to epidemiological surveys who report using opioids without prescriptions also obtain them from friends or relatives (e.g., McCabe 2007), and this seems to be likewise true of people in treatment for opioid dependence (Rosenblum et al., 2007). Unlike illicit drugs, therefore, in which there is a large, global trade, most prescription opioids are obtained locally from physicians and pharmacists.

**Epidemiology of opioid overdose**

According to data from the Drug Abuse Warning Network (DAWN) (Substance Abuse and Mental Health Services Administration, 2002), which collects information from a representative American sample of emergency departments, medical examiners, and coroners, incidents involving opioid analgesics increased 83.5% between 1997 and 2002. More recent DAWN data have shown that overdose deaths resulting from the non-medical use of opioid analgesics now outnumber those due to heroin or cocaine (Paulozzi, 2006). Evidence from the same source has shown that ED contacts for opioid overdose are strongly correlated over time with the total amounts of opioids prescribed in the United States, and that the number of overdose incidents per unit of morphine equivalents prescribed is reasonably similar across all opioids (Dasgupta et al., 2006).

There are limited data on the epidemiology of opioid overdose in Canada. A toxicological study of 251 hydromorphone-related deaths investigated by the coroner's office in Ontario between 1985 and 2003, however, reported that such deaths increased sharply over this period (Wallage & Palmentier 2006). Between 1985 and 1991, there were no more than 2 known fatal cases of hydromorphone poisoning per year. Between 1996 and 2000, there were approximately 20 annually, and in 2003 there were 63.

**Opioid-related harms, prescribing practices, care**

Several studies have linked poor prescribing practices with population-level indicators of harms, particularly overdose. Between 1985 and 1995, the United Kingdom had a substantially higher incidence of fatal methadone overdoses than other countries, and this is thought to have been largely the result of poor practice: During this period, methadone was commonly dispensed in substantial quantities for self-administration. The adoption of guidelines recommending supervised dosing – in which most patients are required to come each day to a pharmacy or specialist clinic to receive methadone – in 1996 led to a substantial decline in mortality (Hall 2000; Strang 2007).

A more relevant example of the association between prescribing practices and opioid-related problems is that of OxyContin. Within a few years of its introduction in 1996, OxyContin had become a significant problem in certain, mostly rural, areas of the United States. The drug's widespread misuse was made possible by inappropriate

local prescribing. The number of prescriptions written by family physicians rose sharply in the late 1990s and early 2000s. This increase has been attributed to aggressive marketing efforts by OxyContin's manufacturer, Purdue Pharmaceuticals, which encouraged physicians to prescribe it for a wide variety of conditions (General Accounting Office, 2003). Primary care physicians, in particular, played an important role, coming to account for almost half of all prescribers of the drug (Van Zee, 2009). OxyContin, however, is only the most prominent example of a much more widespread increase in problems stemming from the expanded use of opioid analgesics.

**Geographical and demographic variation in risk of opioid poisoning**

Opioid poisoning is not uniformly distributed in the population. As with other substance-related problems, there are considerable differences between areas. Availability of these drugs, for example, may vary with jurisdiction or according to variations in practice. Epidemiological research in the United States has also shown that problematic opioid use varies markedly between states (e.g., Kuhn 2007). These between-state differences have been linked to differences in the overall levels of opioid prescribing, which have been shown to vary substantially (Paulozzi & Ryan, 2006).

Existing evidence from the United States suggests that opioid-related problems are, in general, more prevalent in rural areas (GAO 2003). Between 1999 and 2004, fatal narcotic drug poisonings rose by 248% in the most rural areas of the U.S.; by the end

of this period, the incidence of fatal drug poisoning in these areas was comparable to that in major cities, and mortality from prescription opioids specifically was higher than in any other urbanicity-based census category. A review of drug and alcohol-related poisoning deaths in New Mexico from 1994 to 2003 similarly found that, although large cities had the highest overall mortality, deaths involving prescription medications were most common in rural areas (Centers for Disease Control and Prevention 2005). This association was particularly marked for opioids.

To date, major Canadian population health surveys have not collected detailed information on the nonmedical use of prescription drugs; as a result, there is limited information available on the epidemiology of opioid misuse in Ontario. The only available estimates come from OSDUHS, which samples only junior high and secondary school students and which added questions on prescription opioid use only in 2007. Its finding of higher levels of non-medical use in northern Ontario, however, agrees with American reports that problems have been concentrated in rural areas.

Several explanations for the increased prevalence of prescription opioid-related problems in rural areas have been proposed. Heroin and other illicit drugs may be less easily available outside of urban centres, which has suggested to some the existence of an 'untapped market' (GAO, 2003). Although fatal overdoses and severe dependence are sometimes concentrated in large urban centres (e.g., Vancouver's lower east side), problems related to alcohol and illicit drug use, broadly defined, appear to be more prevalent in mid-sized cities and in rural areas (Veldhuizen et al.,

2006). It is conceivable that the higher levels of opioid-related problems in rural areas are, therefore, due in part simply to a higher propensity to use or misuse alcohol and drugs in general. It has been noted that the prevalence of opioid and alcohol-related problems were elevated in Appalachia long before the appearance of OxyContin (GAO, 2003).

**Variations in opioid poisoning in Ontario**

Several factors, then, might give rise to geographical differences in the incidence of opioid overdose. These include differences in the prevalence of health conditions for which opioids are legitimately prescribed; in the quality of medical care provided (e.g., inappropriate prescription, lax monitoring); and in background levels of problematic substance use and of risk factors for problematic substance use.

There is some evidence that specialist physicians are better-placed than general practitioners to treat chronic pain conditions and to manage opioid prescriptions. A Danish study showed that care at a specialist clinic resulted in improvements in functioning and subjective pain, while care dispensed by general practitioners after specialist assessment was significantly less effective (Becker et al., 2000). Non-specialists may also be somewhat more likely to prescribe inappropriate medications generally (Goulding 2004; Nissen 2001), and opioids may be particularly problematic.

Similarly, a recent American survey concluded that guidelines, including those on opioid prescription, were frequently violated in primary care (Di Iorio et al., 2000). Many primary care physicians have doubts about their own expertise in the area of pain management; in a recent British survey, only 11% of practitioners had specialized training in pain management, and 95% of the remainder felt their medical school or primary care training in this area was inadequate (Hutchinson et al., 2006).

Another potential link between rural residence and misuse of opioids, however, concerns the availability of medical services. In Canada, specialist physicians are heavily concentrated in major cities, while general practitioners provide the majority of medical care in rural areas (Pong & Pitblado, 2005). Despite consistent efforts by the provincial government to attract physicians to rural and northern areas, these parts of the province are underserved. Among Ontario's 49 counties, the number of specialist physicians per 100,000 population varies from a low of 0 to a high of over 250 (table 2). These numbers may also obscure a more serious shortage in remote areas, since the impact of the relatively low numbers of specialists in some southern Ontario regions may be ameliorated by the ease of travel to Toronto or other cities for specialist consultations. General practitioners in more remote regions typically serve large numbers of patients scattered across large geographical areas. Since specialists are scarce, general practitioners in these practices are typically responsible for a broader spectrum of medicine than their urban colleagues (CIHI, 2005).

The lack of easily accessible care in rural and remote parts of the province is reflected in statistics on hospitalization rates for conditions that can usually be successfully treated in community settings (known as ambulatory care sensitive conditions, or ACSCs). ACSCs include diabetes, asthma, hypertension, substance dependence, and mood or anxiety disorders that are seldom severe enough to merit hospitalization (e.g., dysthymia, panic disorder, specific phobia) (Statistics Canada, 2004). High levels of hospital admissions for these conditions are thought to indicate limited access to community-based health services, since appropriate management will usually prevent them from becoming severe enough to require inpatient care. In 2004-2005, age standardized rates of hospitalizations for ACSCs per 100,000 varied substantially across Ontario's local health integration networks (LHINs), from 223 in Central to 658 and 694 in the North East and North West LHINs, respectively (CIHI, 2007).

*Table 2. General practitioner and specialist availability (physicians per 100,000 population) in Ontario in 2005 by census division.*

| Census Division | Specialists (n) | Non-specialists (n) | Specialists per 100K | Non-specialists per 100K |
|---|---|---|---|---|
| Algoma | 68 | 112 | 58 | 95 |
| Brant | 79 | 99 | 65 | 81 |
| Bruce | 2 | 49 | 3 | 76 |
| Cochrane | 30 | 93 | 36 | 111 |
| Dufferin | 22 | 40 | 42 | 76 |
| Durham | 274 | 332 | 51 | 62 |
| Elgin | 41 | 57 | 49 | 68 |
| Essex | 251 | 248 | 65 | 65 |
| Frontenac | 359 | 226 | 254 | 160 |
| Grey | 62 | 83 | 68 | 91 |
| Haldimand-Norfolk | 14 | 61 | 13 | 57 |
| Haliburton | 1 | 12 | 6 | 77 |
| Halton | 258 | 352 | 63 | 86 |
| Hamilton-Wentworth | 854 | 432 | 172 | 87 |

| Census Division | Specialists (n) | Non-specialists (n) | Specialists per 100K | Non-specialists per 100K |
|---|---|---|---|---|
| Hastings | 84 | 101 | 66 | 79 |
| Huron | 11 | 47 | 18 | 79 |
| Kenora | 19 | 89 | 30 | 141 |
| Kent | 43 | 64 | 40 | 59 |
| Lambton | 70 | 75 | 55 | 59 |
| Lanark | 20 | 71 | 32 | 112 |
| Leeds & Grenville | 47 | 75 | 48 | 77 |
| Lennox & Addington | 3 | 38 | 8 | 95 |
| Manitoulin | 0 | 19 | 0 | 147 |
| Middlesex | 732 | 380 | 177 | 92 |
| Muskoka | 23 | 69 | 42 | 125 |
| Niagara | 251 | 285 | 60 | 68 |
| Nipissing | 68 | 77 | 81 | 92 |
| Northumberland | 20 | 56 | 25 | 71 |
| Ottawa-Carleton | 1381 | 969 | 174 | 122 |
| Oxford | 33 | 64 | 33 | 63 |
| Parry Sound | 7 | 37 | 17 | 92 |
| Peel | 585 | 770 | 54 | 72 |
| Perth | 52 | 62 | 70 | 84 |
| Peterborough | 116 | 127 | 90 | 98 |
| Prescott & Russell | 24 | 74 | 31 | 94 |
| Prince Edward | 4 | 26 | 16 | 103 |
| Rainy River | 2 | 23 | 9 | 105 |
| Renfrew | 28 | 77 | 29 | 80 |
| Simcoe | 208 | 329 | 52 | 82 |
| Stormont Dundas & Glengarry | 53 | 107 | 48 | 97 |
| Sudbury D.M. | 1 | 12 | 5 | 54 |
| Sudbury R.M. | 164 | 143 | 105 | 91 |
| Thunder Bay | 129 | 143 | 86 | 95 |
| Timiskaming | 10 | 42 | 30 | 124 |
| Toronto Metropolitan | 4261 | 2835 | 171 | 114 |
| Victoria | 24 | 47 | 33 | 65 |
| Waterloo | 285 | 363 | 62 | 79 |
| Wellington | 120 | 169 | 62 | 87 |
| York | 443 | 580 | 55 | 72 |

There are thus a number of reasons to suspect a link between incidence of opioid overdose and availability of specialist medical care. As noted, opioids may be more likely to be inappropriately prescribed by primary care providers in general, and this

may be particularly true in areas where a single provider is responsible for a large number of clients and has limited options for specialist referral. The relative inaccessibility of specialist consultations may mean that diagnosis and effective treatment of painful conditions is more difficult; some imaging services, for example, are available only at a relatively small number of specialized centres. This may lead to long-term management with opioids when other treatments might be possible. Furthermore, distances between providers and patients may also prevent careful management of opioid and other medications. It may be impractical, for example, for a provider in a remote area to see a client as frequently as would be ideal. All of these issues may lead to higher levels of opioid use, and also to a greater potential for misuse or diversion.

These issues may also increase risks of other conditions that frequently contribute to overdose. The same factors affecting management of opioid prescriptions may lead to inappropriate or poorly-managed use of benzodiazepines, which, as described above, frequently contribute to overdose. The high level of ACSCs in these parts of the province may also increase both need for opioids and risk of overdose. Inadequately managed diabetes, for example, may lead to diabetic neuropathy, a painful condition that may require treatment with opioids. At the same time, other conditions, such as liver problems arising from alcohol use or hepatitis, may increase susceptibility to overdose, and these are sometimes avoidable with appropriate medical care.

**Study purpose**

This study has two aims. The first is to describe the epidemiology of opioid poisoning in Ontario in recent years, with attention to trends over time and demographic differences in event rates. The second is to examine a possible link between the availability of specialist care and the rate of opioid poisoning. As noted, previous work has shown that opioid analgesic availability is a function of local prescribing practices, and that these, in turn, often vary sharply between regions. There is also evidence that specialists are better able to manage chronic pain (Becker et al., 2000), are more likely to follow prescribing guidelines (Nissen et al., 2001; Goulding et al., 2000), and are more successful in avoiding medication-related harms. The hypothesis examined in this study is therefore that low availability of specialist physicians is associated with a high incidence of prescription opioid poisonings.

## METHODS

### Data

Data on opioid poisoning episodes were drawn from the National Ambulatory Care Reporting System (NACRS), a database maintained by the Canadian Institute for Health Information (CIHI) which includes episodes of hospital- and community-based ambulatory care. Variables available in the NACRS database are listed in table 3. For this project, we obtained records of all emergency department (ED) admissions in the province of Ontario between April 2002 and March 2006 (i.e., fiscal years 2002 to 2005) for which opioid poisoning was listed as a diagnosis. Diagnosis was determined from the ICD-10 codes recorded for treatment contact; those codes corresponding to opioid poisoning for the purposes of this analysis are listed in table 4. Records were included irrespective of the presence of other diagnoses, even if opioid overdose was not the first condition listed. The most common co-occurring diagnoses are given in table 8, while the most common primary diagnoses in cases where opioid poisoning was listed as a secondary diagnosis are given in table 9. All conditions accounting for 1% or more of the latter records concern either poisoning with other substances (notably acetaminophen and benzodiazepines) or mental health conditions that may be associated with increased risk of substance abuse or deliberate self-harm. Records flagged as 'multiple contact records', which occur when an individual is seen by multiple providers in the context of a single event, were excluded. Poisonings resulting from use as intended are excluded on conceptual and practical grounds, for reasons described below.

Information on total opioid prescriptions dispensed from Ontario pharmacies was obtained from IMS Health.

*Table 3. NACRS variables.*

| |
|---|
| Patient ID |
| Fiscal year |
| Patient's birth year |
| Patient's gender |
| Patient's FSA |
| ICD10 diagnosis codes (up to 25) |
| "Coding class" |
| Admission date |
| Discharge date |
| MCR flag ("to indicate multiple contact records in NACRS") |

**Variables**

The NACRS dataset obtained includes ICD-10 codes providing information about the circumstances in which each poisoning event occurred. Virtually all contacts were accounted for by four types of events: Complications of care due to use of analgesics (ICD-10 code Y45); intentional self-poisoning (X60-X64); poisoning with undetermined intent (Y10-Y14); and accidental poisoning (X40-X44).

*Table 4. ICD-10 diagnostic codes for opioid overdose.*

| | |
|---|---|
| T40.2 | Poisoning by other opioids (codeine, morphine, oxycodone, hydrocodone, hydromorphone) |
| T40.3 | Poisoning by methadone |
| T40.4 | Poisoning by other synthetic narcotics (fentanyl, pethidine) |
| T40.6 | Poisoning by narcotic, not elsewhere classified (other, unknown, or unidentified opioid) |

**Complications of care**

Complications of care are adverse events occurring when medications are taken as prescribed. CIHI coding guidelines state that this event type should not be associated with opioid poisoning codes (CIHI, 2006). In the dataset received, however, there were 1138 admissions with this combination of codes. These records were excluded from the analysis for several reasons. The most important of these is that the included records are likely to represent an unknown proportion of all contacts for adverse events. The number of these events declined substantially over time, from 360 in FY2002 to 221 in FY2005, while all other types of events increased in number. In the absence of very significant, province-wide improvements in the management of opioid medications, this strongly suggests a gradual shift in coding practices. The included data are also not likely to be a random subset of all contacts for adverse events, as their inclusion may have been influenced by differences in practice between hospitals or analysts.

Adverse events occurring when medications are taken as prescribed are also perhaps less likely than other contacts to represent serious overdoses. Mild overdoses or various opioid side effects might lead to an ED visit, and these may have erroneously been recorded as 'poisonings'. Finally, the exclusion of adverse events results in a dataset that should consist entirely of events arising from misuse (principally accidental overdoses and incidents of self-harm). Although inclusion of adverse events would result in a more complete picture of the public health consequences of

prescription opioid use, the set of ED contacts resulting from misuse thus remains conceptually meaningful.

Intentional self-poisonings include events where the overdose was the result of a deliberate attempt at self-harm. Accidental poisonings include overdose due to misuse, but also overdoses occurring due to errors in use of a prescribed medication on the part of a patient, health care provider, or other individual. Events of undetermined intent include all those incidents where an external cause could not be identified. A small number of events received multiple or no flags, and a very small number received other designations (e.g., assault). These were combined with events of undetermined intent to form an 'undetermined or other' category.

Results are therefore reported for three types of events: Accidental overdoses; intentional self-poisonings; and events of undetermined or other intent (including those with no, multiple, or other flags). The multivariable analysis focuses on the total number of events ascribed to accidental overdose or of undetermined or other intent. This approach follows existing work (e.g., Paulozzi, 2006) and is intended to capture events resulting from recreational use.

**Population-level data**

Populations, age distributions, and socioeconomic status indicators are available from census tables and postal code databases published by Statistics Canada and were obtained through the University of Toronto's data library. As these results are

available for the census years of 2001 and 2006, while the study data cover the intervening period, it was necessary to impute populations for each of 10 age/sex groups in each forward sortation area (FSA). This was done by calculating the rate of growth between the two censuses and using this to estimate values for each year between these points. The rate of growth between two (non-zero) measurements is given by the formula $g = [(t_2/t_1)^{(1/n)}] - 1$, where n is the number of intervening time points. The population estimate at each time point is then given by the formula $t_n = t_1 * (1+g)^n$.

The analysis includes 5 categories for age (0 to 14, 15 to 24, 25 to 49, 50 to 64, and 65 and older) and two for sex (male and female), for a total of 10 groups. NACRS data were collapsed to obtain a count of events of each type by FSA and age/sex category, while population counts for each of these groups was obtained as described from census data.

*Table 5. Income, rurality, overdose rates, and physician availability in Ontario (means).*

| | |
|---|---|
| Median household income | $60,455 |
| Proportion rural | 15.3% |
| Illicit drug or alcohol poisoning event rate (annualized, per 100,000) | 12.0 |
| Specialist physicians per 100,000 | 84.7 |
| General practitioners per 100,000 | 92.6 |

**Independent variables**

*Age and sex.* As noted, substantial demographic differences in rates of opioid overdose have been previously reported, and are universally found in population-based investigations of harms related to substance use.

*FSA-level variables*

The multivariable analysis includes 5 variables measured at the FSA or census division level. Provincial averages for these variables are presented in table 5.

*Rural/urban forward sortation area.* Forward sortation areas are classified as either urban or rural; rural FSAs have a zero in the second position of the three-letter FSA identifier (e.g., P0L). Although this distinction is made to indicate the means of mail delivery in each area, and does not reflect any more detailed information on population density, it can be expected to reflect a fair distinction between urban and rural areas, and has the further advantage of providing a binary indicator at the main level of analysis. 55 of the 505 populated FSAs included in the analysis, representing 15.3% of the provincial population, were rural.

*Median household income.* This is a general measure of regional socioeconomic status (SES), which is known to be important in studies of substance-related harms. The Canadian census includes several potential measures of SES, including unemployment rate, proportion of households below a "low income" threshold, and the proportion of individuals with various levels of education. Median household income was selected because it is a continuous measure that will reflect the general level of prosperity or poverty within the region, and because it accounted for more model variance than most other possibilities. Education measures proved at least equally statistically significant in preliminary models, but were also more strongly

correlated with the availability of specialist physicians, and so were avoided partly in the interests of avoiding collinearity.

*Background incidence of overdose*. Background rates of ED visits for non-opioid recreational drug overdoses were obtained from the same NACRS dataset used to derive data about opioid poisonings. This variable is the rate per 100,000 population of all poisonings due to the use of cocaine (ICD 10 code T405), cannabis (T407), ethanol (T510), or hallucinogens (T408, T409). Psychostimulants other than cocaine (e.g., MDMA, methamphetamine, amphetamine) were not included because the ICD-10 code under which they fall (T436) includes prescription stimulants such as methylphenidate, the use of which might be influenced by the same factors (including availability of specialist care) as the primary outcome.

*Availability of general and specialist physician care.* Data on the numbers of specialist and nonspecialist physicians practising in Ontario's regions were obtained from the Ontario Physician Human Resources Data Centre (OPHRDC) report '2005 Physicians In Ontario by Specialty and Region' (OPHRDC, 2006). The present analysis uses counts of physicians at the census division (CD) level, divided by the CD population and multiplied by 100,000 to obtain a measure of specialist and nonspecialist physicians per unit population. Although these data reflect counts only in calendar year 2005, they are likely to be generally representative of the distribution of physicians over the study period as a whole; only substantial shifts in this

distribution between 2002 and 2005 would pose a threat to the validity of this measure.

Ontario includes 49 census divisions. In the 2006 census, these units varied in size from approximately 13,000 (Manitoulin) to 2.5 million people (metropolitan Toronto), with a mean of 248,000 and a median of 103,000. Census divisions cover geographical areas substantial enough for an aggregate measure of availability to be meaningful, but numerous enough for there to be adequate variability. Postal units, however, do not correspond to Statistics Canada regions. Using a file linking postal codes to census regions obtained from DMTI Spatial (DMTI, 2004), it was determined that 109 of the 512 FSAs with non-zero populations, representing approximately 28% of the provincial population in 2006, did not fall within a single CD. In these cases, availability was calculated as an average of the CDs overlapping the FSA, weighted by the population within each CD. This process resulted in an exposure variable with a total of 135 levels. This process was chosen as a reasonably simple and conceptually acceptable way of obtaining a measure of physician availability. Although there are methods of spatial analysis that provide alternative techniques for approaching problems of this kind (e.g., Best et al., 2000), these are complex, of uncertain value, and can complicate the interpretation of results.

## Analysis

### Descriptive epidemiology of opioid poisoning in Ontario

The first part of the analysis concerns the number of poisoning events recorded, their circumstances, trends over time, and demographic differences. In most cases, event rates are preferred to incidences. Event rates are calculated by dividing the total numbers of events by the appropriate interpolated census population. Incidence is similar, but the numerator represents the number of individuals presenting within each period. Event rates are reported for each of 10 demographic categories, as well as for the province as a whole and for each year. Incidence is not calculated for individual types of events largely because the determination of the population at risk becomes somewhat arbitrary and the resulting number correspondingly less meaningful: A single individual with 3 ED visits within a year will be counted once in the calculation of overall annual incidence, but might appear in each of three event-type-specific numerators. Cases where multiple event types are recorded present further complications. In this context, event rates are clearer and more meaningful, as well as more accurately reflecting the clinical and public health burden of opioid poisoning.

### Regression modeling

The multivariable analysis is performed on three outcomes: 1) the total event rate; 2) the rate of accidental events plus the rate of events of undetermined or other intent; and 3) the rate of incidents of self-harm. Modeling is done using a mix of Poisson and negative binomial regression.

Poisson regression is a type of generalized linear model appropriate to count outcomes. Observed counts are assumed to result from Poisson processes, in which events occur independently and continuously. Counts of events resulting from such a process follow a Poisson distribution, which is characterized by a single parameter ($\lambda$) which is equal to both the mean and the variance. Poisson regression models the log of the expected count as the function of an intercept and a vector of coefficients for predictor variables. Where the 'exposure' (i.e., the denominator of the event rate) varies between units of the analysis, the model also includes an offset. The offset is the log of the exposure (in epidemiology, typically people, person-years, or time) and receives a coefficient constrained to equal 1. The general form of a Poisson model for rates is thus:

$$\log(E(Y)) = \log(\text{exposure}) + a + bx$$

Equivalently, the expected count is:

$$E(Y) = \exp(\log(\text{exposure}) + a + bx)$$

A common problem with Poisson models is that observed distributions of counts do not follow a strict Poisson distribution, but rather have a variance greater than the mean. This situation, known as overdispersion, can be interpreted as the result of unknown influences on the underlying process which result in wider-than-expected

variation in rates (StataCorp, 2009). Negative binomial regression is an alternative to Poisson regression that addresses this problem by introducing a model parameter (α) to correct for overdispersion (alternatively, Poisson regression can be defined as a special case of negative binomial regression in which α is fixed to zero). This extra parameter allows the negative binomial distribution to take on a much greater variety of forms.

In the present analysis, Poisson models were fit initially and were tested for overdispersion using *estat gof* in Stata, which compares the fit of a Poisson to that of a negative binomial model and performs a likelihood ratio test to determine whether the inclusion of a dispersion parameter significantly improves model fit (StataCorp, 2009). Where significant overdispersion was present, negative binomial regression was then used. In the results presented, the time-only models were fit using Poisson regression; all others used negative binomial regression. All models were adjusted for the population at risk for each unit of the analysis by specifying the appropriate population variable as the relevant exposure.

Both Poisson and negative binomial regression yield incidence rate ratios (IRR). In the case of binary predictor variables, an IRR may be interpreted as the rate in the "exposed" group divided by the rate in the "unexposed" group. For continuous or ordinal variables, the IRR represents the change in the outcome rate associated with an increase of 1 in the predictor. The expected rate for a given set of variable values can be obtained from the formula $r = \exp(x) / (1+\exp(x))$, where x represents the

solution to the regression equation for the values of interest. This approach was used to generate the graphs of predicted rates presented in figures 3 and 4.

**General approach**

The rates of each of the three event types defined above are analyzed using the following series of models:

1. Event rate = f(time)
2. Event rate = f(age, sex)
3. Event rate = f(age group, sex, urban/rural, median FSA income, rate of drug overdose)
4. Event rate = f(age group, sex, urban/rural, median FSA income, rate of drug overdose, specialist availability, nonspecialist availability)

Model 1 tests for change in the event rate over time. Models 2 through 4 are nested models. Model 2 explores variation by age and sex, while model 3 introduces the FSA-level study variables. Model 4 adds the physician availability variables in order to assess their independent effects on the event rate. It should be noted that the effect for time is omitted from models 2 through 4, and that these models thus examine variation across the other variables throughout the study period as a whole.

**Fractional polynomials**

In this analysis, specialist physician availability is modeled as a continuous variable. Although the study hypothesis posits an inverse association between specialist

availability and the rate of prescription opioid poisoning, it is not certain that the independent association between these two variables, if one exists, is linear at the log scale. An examination of the bivariate relationship between the outcomes and the availability variable (e.g., figure 2) suggested that it was not. This, however, is the only detectable possibility for continuous variables entered into an ordinary Poisson or negative binomial model.

In order to test for a possible non-linear effect for the availability of specialist physicians and to fit parameters reflecting such a relationship, I use the method of fractional polynomials (Royston & Altman, 1994). This approach involves fitting models that include different transformations of the original variable and combinations thereof, and selecting the model which best fits the data. The fractional polynomials procedure used fits powers of -2, -1, -0.5, 0.5, 1, 2, 3, and the natural logarithm. As implemented in Stata 11, models with all possible combinations of terms are fitted and their total deviance compared. Details of this process are available in Stata documentation (StataCorp, 2009). In the present analysis, I fit models of up to 2 terms.

Effects for other continuous covariates were also assessed for linearity. This was done using FP in models including only the covariate of interest. Attempts to fit these terms simultaneously in the full model would be problematic because of the extraordinarily large number of models that would need to be tested and associated problems of computational tractability and complications in questions of statistical

inference arising from large numbers of tests. In the case of nonspecialist availability, a statistically significant improvement ($p=0.04$) was obtained for a term raised to the power of -2, but the practical improvement in model fit was small and appeared not to justify the added complexity. A linear model was therefore used. For median family income, the linear effect was optimal, while a square root transformation was applied to ED contacts for alcohol or illicit drug poisoning.

**Adjustment for clustering of observations**

In models 2, 3, and 4, for which data are aggregated to the level of within-FSA age/sex groups, variance estimation uses the 'cluster' option in Stata. This takes into account shared variance within FSAs. FSA of residence does not otherwise appear in the models used. Investigations of this approach have found that, in addition to improving robustness of standard errors, it presents minimal risks when the number of clusters is greater than 50 (Kezdi, 2004).

All statistical analyses were performed using Stata 11 (StataCorp, 2009), with the exception of frequency distributions, which were calculated using a Microsoft Access database.

**Methodological issues: Statistical testing of 'census' data**

The data used in this analysis represent not a sample, but the total number of observed events for the entire population of interest. Event counts and rates are therefore reported without confidence intervals. The analysis does, however, include

significance tests for changes over time and for associations between variables. The reason for this is that the purpose of the analysis is not to uncover variation in rates, but to test for changes in or influences on the underlying processes that give rise to opioid poisoning events. The question is therefore not whether there are differences in rates between subpopulations or over time, but whether this variation reflects real differences in the likelihood of these events occurring. Despite the fact that they represent a population, therefore, the observed data are treated as a sample of all possible outcomes.

**Methodological issues: Limitations of ecological analysis**

This analysis is an ecological one, in that it tests for an association between a region-level characteristic and the sum or average of many individual outcomes. This type of analysis is valuable in situations, such as this one, where alternative designs are not practical and where regional-level results are of interest, but it has a number of significant limitations. The two most important of these are the 'ecological fallacy' and the 'modifiable unit area problem'. The ecological fallacy refers to problems with drawing conclusions about individual-level characteristics from group-level measurements. A common example of this issue is the correlation between wealth and obesity, which is positive when variation between countries is considered but tends to be inverse in single-country, individual-level data. In the present context, there may be important geographical differences that are influencing the apparent association between availability of care and opioid poisoning rates. The modifiable unit area problem refers to errors in statistical inference that can arise when spatial

data are aggregated. The essential issue is that redrawing boundaries between areas can cause observed correlations, or multiple regression coefficients, to vary substantially.

These issues affect the majority of ecological analyses. In the present context, there are no practical alternatives to the analysis done, in the absence of considerably more detailed data than are available. The relatively large number of units of analysis may, moreover, provide some protection from these issues.

**Single-level v. multilevel models**

Populations at risk and counts of events are aggregated to the level of age/sex groups within FSAs, and the nesting of these records within FSAs is taken into account, as noted, by the specification of FSAs as clusters in the analysis. This approach does not, however, explicitly model FSA-level differences in the processes giving rise to poisoning events. This could be done using mixed effects models, which would permit the inclusion of random effects. A random intercept at the FSA level in such a model would make it possible to model this variation, while random effects for predictors could take into account between-FSA differences in their effects.

To evaluate this approach, a mixed effects Poisson model was fit for the final model of total events, with a random intercept at the FSA level. The random effect parameter was substantial (beta=0.425, SE=0.02), indicating the existence of considerable regional variation otherwise unaccounted for in the analysis. Parameter

estimates for fixed effects, however, were very similar to those obtained from the single-level model, with the majority within 10% of the single-level estimates and none differing by more than 15%. It is also not certain that results from the mixed effects Poisson model are more accurate than those from the single-level negative binomial model, as the former did not take overdispersion into account. Given that the explicit modeling of FSA-level effects was not a goal of the analysis, that the improvements in accuracy are uncertain, and that a multilevel approach would add considerable complexity to the analysis and to the interpretation of results, therefore, single-level models were used throughout the analysis.

## Results

### Descriptive epidemiology

Between April 2002 and March 2006, there were 6283 ED contacts for opioid poisoning arising from incidents of self-harm, accidental overdose, or of other or undetermined causes. These visits were made by 5647 different individuals. 1962 events (31%) were judged to be due to accidental overdose and 2764 (44%) to intentional self-harm. For 1475 (23.5%) events, intent was recorded as 'undetermined'. The remaining 82 events received multiple, other, or no event codes. For the purposes of the analysis, the 1557 events in the latter two groups were combined into a single 'undetermined or other' category. 1138 contacts in the data received were due to complications of care and were excluded from further analysis. Event counts and rates are presented in table 6.

The total number of events rose each year, from 1250 in FY2002 to 1816 in FY2005. Event rates are given in table 6 and are plotted in figure 1. Annual incidence for the province rose from 10.2 per 100,000 in FY2002 to 14.3 per 100,000 in FY2005. This corresponds to an overall increase of 40%, or an annualized increase of 11.8%. Between FY2002 and FY2005, the total number of events rose 30% for self-harm, 56% for undetermined or other, and 60% for accidental overdose. Event and incidence rates varied substantially by age, peaking among people aged 25 to 49, but were very similar for men and women (tables 7a and 7b).

There was marked variation between age groups and sexes in the types of events recorded. Events occurring in women were more likely to be deemed the result of intentional self harm, while events of undetermined intent were somewhat more common among men and accidents were equally common in both sexes. Accidental overdoses predominated among children under 15. Variation among age/sex groups was generally highly significant (table 12).

*Table 6. Total events and events per unit population, by year.*

| | FY2002 | FY2003 | FY2004 | FY2005 |
|---|---|---|---|---|
| **Opioid poisoning events** | | | | |
| Accidental | 373 | 459 | 528 | 602 |
| Undetermined or other | 291 | 388 | 424 | 454 |
| Total accidental, undetermined, or other | 664 | 847 | 952 | 1056 |
| Self-harm | 586 | 708 | 710 | 760 |
| Total | 1250 | 1555 | 1662 | 1816 |
| **Events per 100,000 population** | | | | |
| Accidental | 3.2 | 4.0 | 4.5 | 5.1 |
| Undetermined or other | 2.5 | 3.3 | 3.6 | 3.8 |
| Total accidental, undetermined, or other | 5.7 | 7.3 | 8.1 | 8.9 |
| Self-harm | 5.1 | 6.1 | 6.0 | 6.4 |
| Total | 10.9 | 13.4 | 14.1 | 15.2 |

*Table 7a. Opioid poisonings by age and fiscal year for men (events per 100,000 population).*

| Event Type | 0 to 14 | 15 to 24 | 25 to 49 | 50 to 64 | 65+ |
|---|---|---|---|---|---|
| FY2002 | | | | | |
| Accident | 3.5 | 2.2 | 3.5 | 2.5 | 4.1 |
| Self-harm | s | 4.2 | 7.7 | 4.2 | 1.7 |
| Undetermined or other | s | 1.9 | 4.3 | 1.8 | 0.9 |
| Total | 3.8 | 8.3 | 15.6 | 8.4 | 6.7 |
| FY2003 | | | | | |
| Accident | 2.4 | 3.6 | 4.0 | 2.9 | 5.5 |
| Self-harm | s | 6.0 | 9.1 | 4.3 | 0.7 |
| Undetermined or other | s | 3.6 | 5.9 | 3.0 | 2.1 |
| Total | 2.5 | 13.1 | 19.0 | 10.3 | 8.3 |
| FY2004 | | | | | |
| Accident | 2.0 | 3.6 | 5.6 | 4.1 | 3.9 |
| Self-harm | s | 5.7 | 9.9 | 4.6 | 2.5 |
| Undetermined or other | s | 4.8 | 6.5 | 3.6 | 2.3 |
| Total | 2.3 | 14.1 | 21.9 | 12.2 | 8.7 |
| FY2005 | | | | | |
| Accident | 2.8 | 4.4 | 6.5 | 4.0 | 6.0 |
| Self-harm | s | 6.8 | 8.9 | 4.6 | 1.7 |
| Undetermined or other | s | 3.1 | 6.8 | 3.5 | 2.3 |
| Total | 3.3 | 14.3 | 22.3 | 12.1 | 9.9 |

[s] Suppressed due to low number of events.

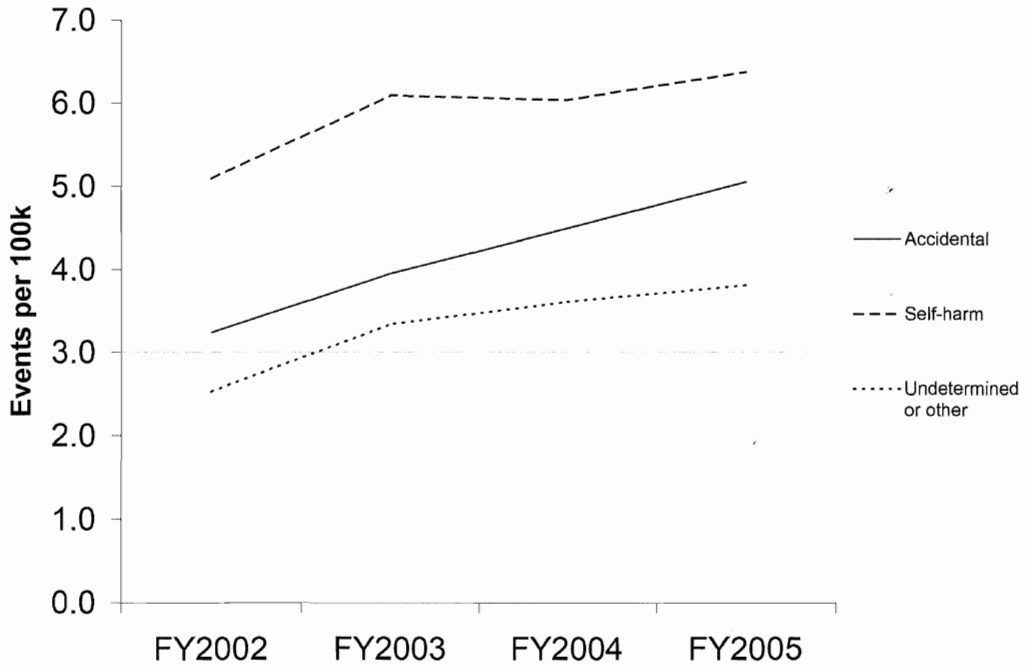
*Table 7b. Opioid poisonings by age and fiscal year for women (events per 100,000 population).*

| Event Type | 0 to 14 | 15 to 24 | 25 to 49 | 50 to 64 | 65+ |
|---|---|---|---|---|---|
| FY2002 | | | | | |
| Accident | 1.6 | 3.3 | 2.8 | 2.8 | 4.9 |
| Self-harm | 0.5 | 9.3 | 7.8 | 4.5 | 1.3 |
| Undetermined or other | s | 3 | 3.2 | 3 | 1.9 |
| Total | 2.3 | 15.6 | 13.8 | 10.3 | 8 |
| FY2003 | | | | | |
| Accident | 2.5 | 4.5 | 3.9 | 4.1 | 4.8 |
| Self-harm | 0.9 | 11.5 | 9.6 | 5.2 | 1.3 |
| Undetermined or other | s | 3.6 | 4 | 2.3 | 2.9 |
| Total | 3.5 | 19.6 | 17.5 | 11.6 | 8.9 |
| FY2004 | | | | | |
| Accident | 2.5 | 3 | 4.7 | 4.4 | 6.6 |
| Self-harm | 1 | 8.5 | 9.2 | 5 | 0.8 |
| Undetermined or other | 0.4 | 3.4 | 3.6 | 3.4 | 2.2 |
| Total | 3.9 | 15 | 17.5 | 12.8 | 9.6 |
| FY2005 | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Accident | 1.1 | 4.4 | 5.1 | 4.9 | 6.9 |
| Self-harm | 1 | 9.7 | 10.4 | 5.7 | 2.1 |
| Undetermined or other | s | 4.1 | 4.3 | 4.3 | 2.1 |
| Total | 2.4 | 18.3 | 19.9 | 14.9 | 11.1 |

[s] Suppressed due to low number of events.

Figure 1. Opioid poisonings per 100,000 population by year and cause.




As noted, ICD-10 includes four codes for opioid poisonings (table 4), but, with the exception of methadone, does not provide information on specific drugs. Across the study period as a whole, 3788 (60%) events were coded as 'other opioids', 1572 (25%) as 'narcotics not elsewhere classified', 746 (12%) as methadone, and 268 (4%) as 'other synthetic narcotics'. Multiple opioid drug classes were recorded in 89 (1.4%) of events.

Diagnoses indicating poisoning due to substances other than opioid analgesics, defined as the presence of one or more other ICD-10 codes between T36 and T50 ("poisoning by drugs, medicaments and biological substances"), were present in 2215 (35%) events. The inclusion of alcohol poisoning (T510, "toxic effects of ethanol")

increases this total to 2298 (37%). 310 (5%) events involved opium, heroin, cocaine, cannabis, or hallucinogens such as LSD or psilocybin (ICD-10 codes between T400 and T409, excluding prescription opioid codes) and 105 (1.7%) included psychostimulants other than cocaine (T436). 434 (7%) contacts had diagnoses of poisoning due to antidepressant or antipsychotic medications. Of these, antidepressants were noted in 361 (6% of total) events and antipsychotics in 105 (1.7%). A corresponding figure for mood stabilizers could not be obtained because the relevant ICD-10 codes largely do not permit the separation of these drugs from (other) anticonvulsant and sedative/hypnotic medications. The most common specific drug-related diagnostic codes recorded were those indicating poisoning due to benzodiazepines (13% of cases), acetaminophen (12%), and cocaine (4%). A list of specific codes and frequencies is presented in table 7.

*Table 8. Most common non-opioid-related ICD-10 diagnoses among people presenting with opioid poisoning (all where proportion of total >1%)*[1].

| ICD-10 code | Description | Occurrences (%) |
|---|---|---|
| T424 | Poisoning: Benzodiazepines | 812 (13) |
| T391 | Poisoning: 4-Aminophenol derivatives (acetaminophen) | 730 (12) |
| F329 | Depressive episode, unspecified | 329 (5) |
| T405 | Poisoning: Cocaine | 233 (4) |
| T432 | Poisoning: Other and unspecified antidepressants | 224 (4) |
| T510 | Toxic effects of ethanol | 200 (3) |
| T430 | Poisoning: Tricyclic and tetracyclic antidepressants | 149 (2) |
| F100 | Acute intoxication | 149 (2) |
| T509 | Poisoning: Other and unspecified drugs and substances | 148 (2) |
| T393 | Poisoning: Other NSAIDs (excludes ASA, acetaminophen) | 126 (2) |
| T450 | Poisoning: Antiallergy and antiemetic drugs | 112 (2) |
| T436 | Poisoning: Psychostimulants with abuse potential (excludes cocaine) | 106 (2) |
| T407 | Poisoning: Cannabis and derivatives | 85 (1) |
| T435 | Poisoning: Other and unspecified antipsychotics and neuroleptics | 84 (1) |
| F101 | Harmful use of psychoactive substances | 82 (1) |
| F432 | Adjustment disorders | 71 (1) |
| T426 | Poisoning: Other antiepileptics and sedative-hypnotic drugs | 63 (1) |

[1] Excludes codes beginning with X and Y (causes of event), U (special-purpose codes), and R (symptoms, signs, and laboratory findings).

*Table 9. First-listed diagnoses where opioid poisoning was given as a secondary condition (all where proportion of total >1%)[1].*

| ICD-10 code | Description | Occurrences (%) |
|---|---|---|
| T391 | Poisoning: 4-Aminophenol derivatives (acetaminophen) | 396 (17) |
| T424 | Poisoning: Benzodiazepines | 324 (14) |
| F329 | Depressive episode, unspecified | 132 (6) |
| T405 | Poisoning: Cocaine | 96 (4) |
| T432 | Poisoning: Other and unspecified antidepressants | 61 (3) |
| T430 | Poisoning: Tricyclic and tetracyclic antidepressants | 58 (3) |
| T393 | Poisoning: Other NSAIDs (excludes ASA, acetaminophen) | 38 (2) |
| F100 | Acute intoxication | 35 (2) |
| F432 | Adjustment disorders | 34 (1) |
| F430 | Acute stress reaction | 30 (1) |
| T510 | Toxic effects of ethanol | 29 (1) |
| T435 | Poisoning: Other and unspecified antipsychotics and neuroleptics | 26 (1) |
| T450 | Poisoning: Antiallergy and antiemetic drugs | 25 (1) |
| T426 | Poisoning: Other antiepileptics and sedative-hypnotic drugs | 23 (1) |
| F191 | Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances | 22 (1) |

[1] Excludes codes beginning with X and Y (causes of event), U (special-purpose codes), and R (symptoms, signs, and laboratory findings).

**Regression results**

Models including time only revealed that trends are highly significant for all event types (table 10). Incidence rate ratios (per year) were 1.11 (95%CI=1.08 to 1.15) for the total count of events, 1.07 (95%CI=1.03 to 1.10) for incidents of self-harm, 1.13 (95%CI=1.08 to 1.18) for events of undetermined or other causes, and 1.15 (1.11 to 1.20) for accidental poisonings. Accidental poisonings and poisonings of undetermined intent thus grew at approximately twice the rate of incidents of self-harm.

*Table 10. Tests for trends for events by type: Incidence rate ratios for year from time-only Poisson regression models.*

| | IRR | IRR L95% | IRR U95% | P |
|---|---|---|---|---|
| Total | 1.11 | 1.08 | 1.15 | <0.001 |
| Accidental | 1.15 | 1.11 | 1.20 | <0.001 |
| Self-harm | 1.07 | 1.03 | 1.10 | <0.001 |
| Undetermined, other | 1.13 | 1.08 | 1.18 | <0.001 |

Models including sex only revealed no difference between the sexes (IRR=1.02, p=0.57) in total event rates. This obscures differences in types of events, however, with self-harm modestly but significantly more common among women and undetermined/other events more common among men (table 11). Differences among individual age/sex groups, which were compared to men aged 25 to 49, were generally highly significant (table 12). All three outcomes were least common among children under 15, while accidental or undetermined poisonings were most common among men aged 25 to 49 (the reference category) and incidents of deliberate self-harm were equally common in this group and among women between 15 and 49. All outcomes became somewhat less common in later life, self-harm particularly so: IRRs among men and women aged 65 or older were 0.17 and 0.14, respectively. Results of models including demographic categories, rurality, income, and non-opioid substance poisonings are presented in tables 13a, 13b, and 13c.

*Table 11. Tests for gender differences by event type: Incidence rate ratios for gender from gender-only negative binomial regression models (females relative to males).*

| | IRR | IRR L95% | IRR U95% | P |
|---|---|---|---|---|
| Total | 1.02 | 0.96 | 1.08 | 0.57 |
| Accidental | 0.97 | 0.89 | 1.07 | 0.59 |
| Self-harm | 1.17 | 1.07 | 1.27 | <0.001 |
| Undetermined, multiple, other | 0.83 | 0.74 | 0.92 | 0.001 |

*Table 12. Tests for differences among age/sex groups (model 2): Incidence rate ratios from age/sex-only negative binomial regression models (reference group = males 25 to 49).*

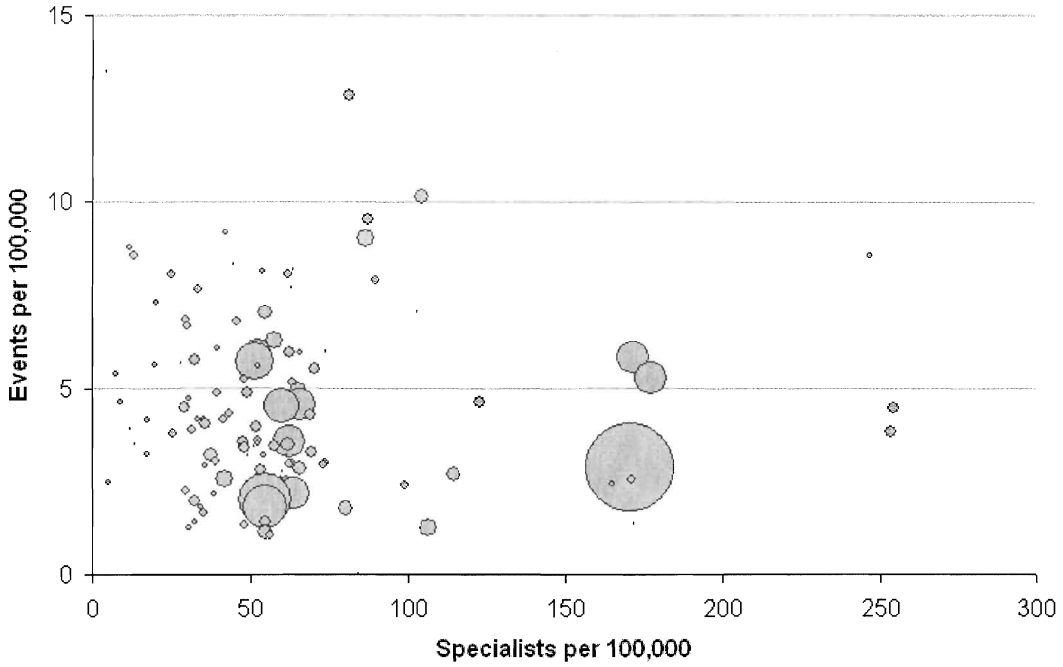
| | Total | | Accidental, undetermined, or other | | Self-harm | |
|---|---|---|---|---|---|---|
| | IRR (95% CI) | p | IRR (95% CI) | p | IRR (95% CI) | P |
| Males | | | | | | |
| 0 to 14 | 0.14 (0.12 - 0.18) | <0.001 | 0.25 (0.21 - 0.31) | <0.001 | 0.01 (0.01 - 0.03) | <0.001 |
| 15 to 24 | 0.62 (0.54 - 0.71) | <0.001 | 0.61 (0.51 - 0.72) | <0.001 | 0.62 (0.52 - 0.75) | <0.001 |
| 25 to 49 | (Reference) | | (Reference) | | (Reference) | |
| 50 to 64 | 0.50 (0.45 - 0.57) | <0.001 | 0.54 (0.47 - 0.63) | <0.001 | 0.46 (0.39 - 0.55) | <0.001 |
| 65+ | 0.39 (0.34 - 0.46) | <0.001 | 0.59 (0.49 - 0.7) | <0.001 | 0.17 (0.12 - 0.25) | <0.001 |
| Females | | | | | | |
| 0 to 14 | 0.15 (0.13 - 0.18) | <0.001 | 0.20 (0.16 - 0.25) | <0.001 | 0.09 (0.07 - 0.13) | <0.001 |
| 15 to 24 | 0.84 (0.75 - 0.94) | 0.003 | 0.66 (0.56 - 0.77) | <0.001 | 1.07 (0.92 - 1.24) | 0.41 |
| 25 to 49 | 0.86 (0.79 - 0.93) | <0.001 | 0.71 (0.64 - 0.79) | <0.001 | 1.03 (0.92 - 1.15) | 0.61 |
| 50 to 64 | 0.59 (0.52 - 0.67) | <0.001 | 0.63 (0.55 - 0.73) | <0.001 | 0.54 (0.45 - 0.65) | <0.001 |
| 65+ | 0.43 (0.38 - 0.49) | <0.001 | 0.69 (0.6 - 0.8) | <0.001 | 0.14 (0.1 - 0.19) | <0.001 |

As noted, examination of the bivariate association between availability of specialist care and opioid poisoning (figure 2) indicated a generally inverse relationship. A small number of data points were at high levels of both variables, implying a possible U-shaped association. Results from full models are presented in tables 14a, 14b, and 14c.

*Table 13a. Results from negative binomial regression model 3 predicting total opioid poisoning events.*

| | IRR | t | p | IRR L95% | IRR U95% |
|---|---|---|---|---|---|
| Males | | | | | |
| 0 to 14 | 0.16 | -18.84 | <0.001 | 0.13 | 0.19 |
| 15 to 24 | 0.65 | -6.45 | <0.001 | 0.57 | 0.74 |
| 25 to 49 | | | Reference | | |
| 50 to 64 | 0.53 | -10.33 | <0.001 | 0.47 | 0.60 |
| 65+ | 0.40 | -11.90 | <0.001 | 0.34 | 0.47 |
| Females | | | | | |
| 0 to 14 | 0.16 | -19.17 | <0.001 | 0.14 | 0.20 |
| 15 to 24 | 0.88 | -2.27 | 0.02 | 0.78 | 0.98 |
| 25 to 49 | 0.89 | -2.75 | 0.01 | 0.82 | 0.97 |
| 50 to 64 | 0.62 | -7.93 | <0.001 | 0.55 | 0.70 |
| 65+ | 0.44 | -12.82 | <0.001 | 0.39 | 0.50 |
| Non-opioid drug overdoses | 1.33 | 11.81 | <0.001 | 1.27 | 1.40 |
| Rural | 1.11 | 1.45 | 0.15 | 0.96 | 1.28 |
| Family median income (per $10,000) | 0.89 | -7.09 | <0.001 | 0.86 | 0.92 |

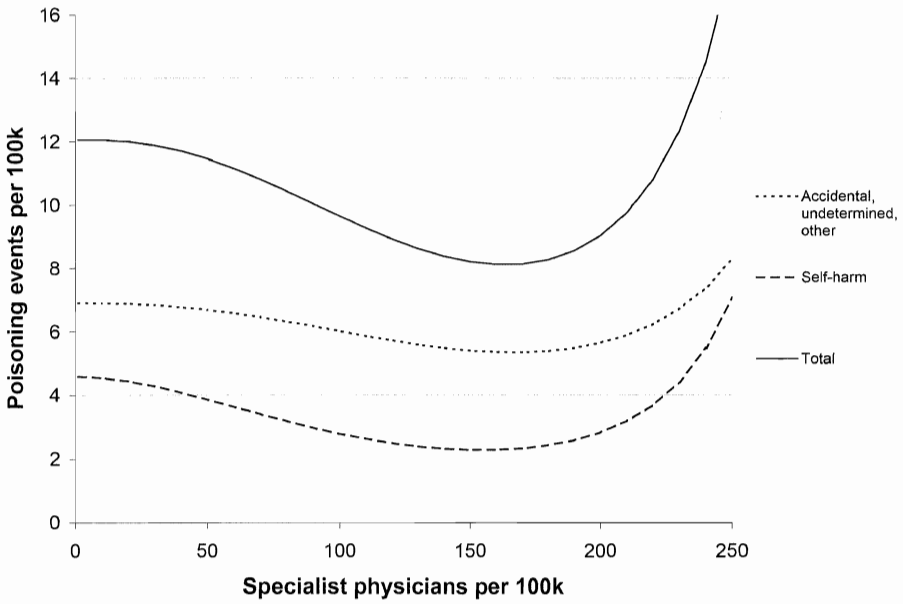
Figure 2. Rates of contacts for opioid poisoning due to accidental, undetermined, or other causes by specialist availabililty (dots sized by population represented).




This association was borne out by results from the full models; for all three outcomes, two polynomial terms proved optimal. Figure 3 shows the predicted rate of poisoning

events of each type across levels of specialist availability with other variables held to their means. In all three models, this relationship is non-linear, with a decrease in poisonings with greater availability of specialist care at low levels of the latter variable transitioning to an increase at higher concentrations of specialists. The magnitude of the association was stronger for incidents of self-harm and total incidents than for accidental, undetermined, and other events. All three functions reach minima between 150 and 200 specialist physicians per 100,000 population.

Figure 3. Predicted rates of opioid poisonings across levels of specialist availability from full negative binomial regression models.




Median family income was inversely and significantly associated with rates of opioid poisoning in all models, while rurality was non-significant in all cases. Effects for rates of ED use for illicit drug or alcohol poisoning, which, as noted, was modeled using a square root transformation, were significant and positive for all three outcomes. Predicted rates for all outcomes across levels of this variable with all

others held to their means are shown in figure 4. The middle 90% of the distribution of FSA-level poisoning rates are included in this figure.

Interactions between the specialist care variables and rurality, non-opioid drug overdose rate, and median family income were explored and proved to be non-significant in all models.

*Table 13b. Results from negative binomial regression model 3 predicting accidental, undetermined, or other events.*

| | IRR | t | p | IRR L95% | IRR U95% |
|---|---|---|---|---|---|
| Males | | | | | |
| 0 to 14 | 0.27 | -12.49 | <0.001 | 0.22 | 0.33 |
| 15 to 24 | 0.63 | -5.31 | <0.001 | 0.54 | 0.75 |
| 25 to 49 | | | Reference | | |
| 50 to 64 | 0.57 | -7.37 | <0.001 | 0.49 | 0.66 |
| 65+ | 0.59 | -5.98 | <0.001 | 0.50 | 0.70 |
| Females | | | | | |
| 0 to 14 | 0.21 | -14.11 | <0.001 | 0.17 | 0.26 |
| 15 to 24 | 0.68 | -4.83 | <0.001 | 0.58 | 0.80 |
| 25 to 49 | 0.74 | -5.56 | <0.001 | 0.66 | 0.82 |
| 50 to 64 | 0.66 | -5.58 | <0.001 | 0.57 | 0.77 |
| 65+ | 0.70 | -5.04 | <0.001 | 0.60 | 0.80 |
| Non-opioid drug overdoses | 1.33 | 11.22 | <0.001 | 1.27 | 1.40 |
| Rural | 1.06 | 0.76 | 0.45 | 0.91 | 1.25 |
| Family median income (per $10,000) | 0.88 | -6.97 | <0.001 | 0.85 | 0.91 |

*Table 13c. Results from negative binomial regression model 3 predicting events due to intentional self-harm.*

| | IRR | t | p | IRR L95% | IRR U95% |
|---|---|---|---|---|---|
| Males | | | | | |
| 0 to 14 | 0.01 | -10.44 | <0.001 | 0.01 | 0.03 |
| 15 to 24 | 0.65 | -4.78 | <0.001 | 0.54 | 0.77 |
| 25 to 49 | | | Reference | | |
| 50 to 64 | 0.48 | -8.29 | <0.001 | 0.41 | 0.57 |
| 65+ | 0.17 | -9.95 | <0.001 | 0.12 | 0.25 |
| Females | | | | | |
| 0 to 14 | 0.10 | -13.18 | <0.001 | 0.07 | 0.14 |
| 15 to 24 | 1.11 | 1.34 | 0.18 | 0.95 | 1.28 |
| 25 to 49 | 1.07 | 1.19 | 0.23 | 0.96 | 1.19 |
| 50 to 64 | 0.57 | -6.44 | <0.001 | 0.48 | 0.67 |
| 65+ | 0.14 | -12.71 | <0.001 | 0.10 | 0.19 |
| Non-opioid drug overdoses | 1.35 | 9.82 | <0.001 | 1.27 | 1.44 |

| | | | | | |
|---|---|---|---|---|---|
| Rural | 1.19 | 1.97 | 0.05 | 1.00 | 1.42 |
| Family median income (per $10,000) | 0.89 | -4.91 | <0.001 | 0.85 | 0.93 |

*Figure 4. Predicted rates of opioid poisonings across levels of illicit drug or alcohol poisonings from full negative binomial regression models.*

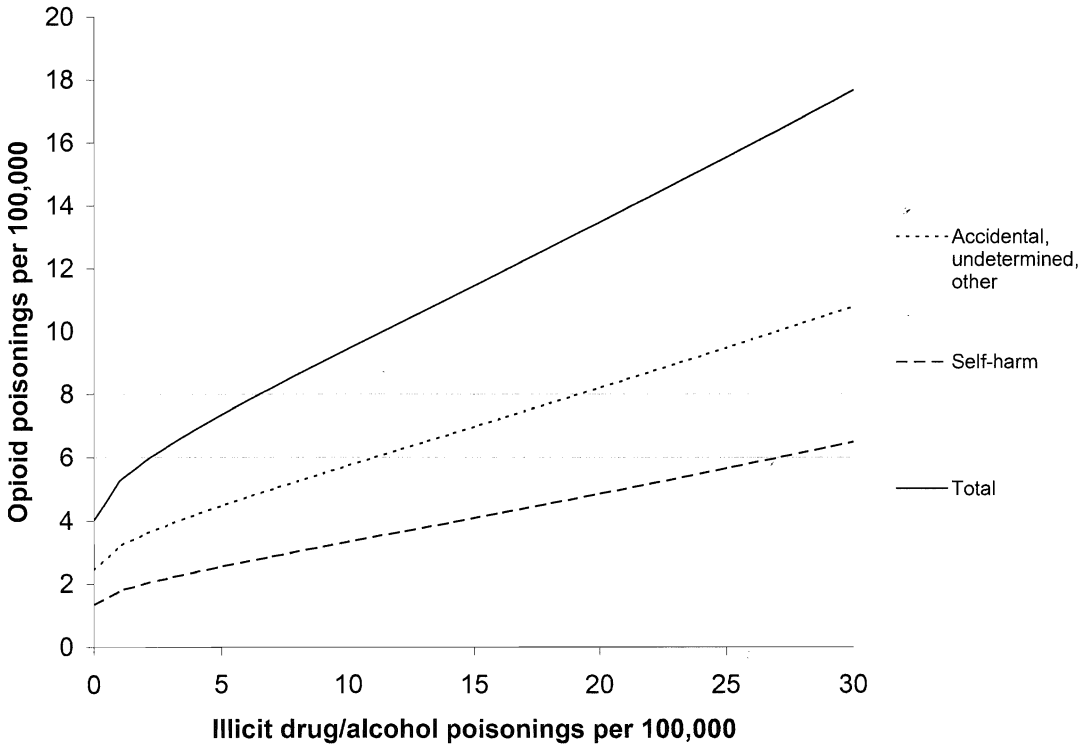


*Table 14a. Results of full negative binomial regression model 4 predicting total number of events across study period.*

| | IRR | t | p | IRR L95% | IRR U95% |
|---|---|---|---|---|---|
| Specialists per 1000[a] | 0.80 | -6.25 | <0.001 | 0.74 | 0.86 |
| Specialists per 1000[b] | 1.31 | 6.89 | <0.001 | 1.21 | 1.42 |
| Nonspecialists per 100k | 1.00 | 0.01 | 0.995 | 0.996 | 1.004 |
| Males | | | | | |
| 0 to 14 | 0.16 | -18.91 | <0.001 | 0.13 | 0.19 |
| 15 to 24 | 0.64 | -6.60 | <0.001 | 0.56 | 0.73 |
| 25 to 49 | | | Reference | | |
| 50 to 64 | 0.53 | -10.54 | <0.001 | 0.47 | 0.59 |
| 65+ | 0.40 | -11.95 | <0.001 | 0.34 | 0.46 |
| Females | | | | | |
| 0 to 14 | 0.16 | -19.28 | <0.001 | 0.14 | 0.20 |
| 15 to 24 | 0.87 | -2.33 | 0.02 | 0.78 | 0.98 |
| 25 to 49 | 0.89 | -2.81 | 0.01 | 0.82 | 0.97 |
| 50 to 64 | 0.62 | -7.98 | <0.001 | 0.55 | 0.70 |
| 65+ | 0.44 | -12.96 | <0.001 | 0.38 | 0.49 |
| Non-opioid drug overdoses | 1.31 | 10.63 | <0.001 | 1.25 | 1.38 |
| Rural | 0.99 | -0.18 | 0.86 | 0.85 | 1.14 |
| Family median income (per $10,000) | 0.87 | -8.35 | <0.001 | 0.84 | 0.90 |

[a] $(\text{Availability}/100)^3$

[b] $(\text{Availability}/100)^3 - \ln(\text{Availability}/100)$

*Table 14b. Results of full negative binomial regression model 4 predicting total number of accidental, undetermined, or other events across study period.*

| | IRR | T | P | IRR L95% | IRR U95% |
|---|---|---|---|---|---|
| Specialists per 1000[a] | 0.87 | -3.25 | 0.001 | 0.80 | 0.95 |
| Specialists per 1000[b] | 1.18 | 3.35 | 0.001 | 1.07 | 1.30 |
| Nonspecialists per 100k | 1.00 | -0.19 | 0.85 | 0.99 | 1.004 |
| Males | | | | | |
| 0 to 14 | 0.27 | -12.54 | <0.001 | 0.22 | 0.33 |
| 15 to 24 | 0.63 | -5.40 | <0.001 | 0.53 | 0.75 |
| 25 to 49 | | | Reference | | |
| 50 to 64 | 0.57 | -7.42 | <0.001 | 0.49 | 0.66 |
| 65+ | 0.59 | -6.03 | <0.001 | 0.50 | 0.70 |
| Females | | | | | |
| 0 to 14 | 0.21 | -14.21 | <0.001 | 0.17 | 0.26 |
| 15 to 24 | 0.68 | -4.83 | <0.001 | 0.58 | 0.80 |
| 25 to 49 | 0.74 | -5.53 | <0.001 | 0.66 | 0.82 |
| 50 to 64 | 0.66 | -5.62 | <0.001 | 0.57 | 0.76 |
| 65+ | 0.69 | -5.12 | <0.001 | 0.60 | 0.80 |
| Non-opioid drug overdoses | 1.31 | 10.24 | <0.001 | 1.24 | 1.38 |
| Rural | 0.98 | -0.29 | 0.77 | 0.82 | 1.15 |
| Family median income (per $10,000) | 0.87 | -7.59 | <0.001 | 0.83 | 0.90 |

[a] $(\text{Availability}/100)^3$

[b] $(\text{Availability}/100)^3 - \ln(\text{Availability}/100)$

*Table 14c. Results of full negative binomial regression model 4 predicting total number of self-harm events across study period.*

| | IRR | t | P | IRR L95% | IRR U95% |
|---|---|---|---|---|---|
| Specialists per 1000[a] | 0.41 | -7.50 | <0.001 | 0.33 | 0.52 |
| Specialists per 1000[b] | 1.46 | 6.91 | <0.001 | 1.31 | 1.63 |
| Nonspecialists per 100k | 1.00 | 0.46 | 0.65 | 0.997 | 1.01 |
| Males | | | | | |
| 0 to 14 | 0.01 | -10.46 | <0.001 | 0.01 | 0.03 |
| 15 to 24 | 0.64 | -4.93 | <0.001 | 0.53 | 0.76 |
| 25 to 49 | | | Reference | | |
| 50 to 64 | 0.47 | -8.58 | <0.001 | 0.40 | 0.56 |
| 65+ | 0.17 | -10.02 | <0.001 | 0.12 | 0.24 |
| Females | | | | | |
| 0 to 14 | 0.10 | -13.26 | <0.001 | 0.07 | 0.14 |
| 15 to 24 | 1.10 | 1.24 | 0.22 | 0.95 | 1.27 |
| 25 to 49 | 1.06 | 1.04 | 0.30 | 0.95 | 1.18 |
| 50 to 64 | 0.56 | -6.57 | <0.001 | 0.47 | 0.66 |
| 65+ | 0.14 | -12.79 | <0.001 | 0.10 | 0.19 |
| Non-opioid drug overdoses | 1.33 | 8.72 | <0.001 | 1.25 | 1.42 |
| Rural | 1.01 | 0.13 | 0.90 | 0.85 | 1.21 |
| Family median income (per $10,000) | 0.88 | -6.19 | <0.001 | 0.84 | 0.91 |

[a] $(\text{Availability}/100)^2$
[b] $(\text{Availability}/100)^3$

## Discussion

Opioids are medically necessary, and their increased use has arisen in part due to well-intentioned efforts to promote their use for the relief of severe pain. A large body of evidence now demonstrates, however, that increases in general availability have been accompanied by increases in non-medical use. Existing work from large-scale studies in the United States has shown that fatal and non-fatal overdose from prescription opioid use has become a significant public health issue over the past twenty years (Paulozzi, 2006; Dasgupta, 2006). Similarly, research in Canada has found that non-medical use of prescription opioids is now reported by substantial proportions of people with substance-related problems (e.g., Fischer et al., 2005) and is now not uncommon in the general population (e.g., Adlaf & Paglia-Boak, 2007). Canadian population surveys have only recently begun to inquire about use of prescription opioids, which makes judgements about recent changes difficult. The fact that this information is now collected at all, however, is symptomatic of the increasing concern surrounding this issue.

### Epidemiology of opioid poisoning in Ontario

Perhaps the most robust finding in the present analysis is the substantial increases in incidence and event rates over time: Year over year, all categories of events increased substantially and, with one minor exception, monotonically, with a total increase in rates for all included poisonings of approximately 40% over a 4 year period. This corresponds to an annualized increase of 11.8%. Although the baseline rate, at approximately 1 event per 1000 people per year, is relatively low, such a change is

nevertheless remarkable. While it would be a mistake to extrapolate from the end of the study period to the present or beyond, it is also clear that the level of poisonings had not stabilized by 2005.

**Risk and public health burden**

In 2005, there were 1056 incidents potentially arising from intentional misuse of prescription opioids, and a further 760 events due to deliberate self-harm. By the end of the study period, there were approximately 1.5 events per 10,000 people per year in Ontario. By way of comparison, there were approximately 200 total ED contacts per 1000 people in 2000 (Chan et al., 2001). Overdose on prescription opioids thus appears to account for very approximately 0.075% of ED visits in the province. Depending on the severity of the poisoning cases, however – on which there is little available information – the clinical burden may be higher than this figure suggests.

Across the study period, poisonings involving opioid analgesics outnumbered those due to all illicit drugs combined. There were 5275 incidents involving cocaine, heroin, opium, cannabis, or hallucinogens, and a further 1956 due to "stimulants with abuse potential" (a category including prescription stimulants, methamphetamine, and MDMA). Although incidents of self-harm may be partly responsible for the preponderance of prescription opioids in ED data, accidental overdoses alone make up a large proportion of all poisonings. These results also bear out existing studies that have shown a displacement of heroin by prescription opioids. Over the study

period, there were 6283 incidents of opioid analgesic overdose and 236 of heroin poisoning, a ratio of approximately 27 to 1.

A very rough assessment of risk relative to exposure is made possible by comparing the volume of drugs dispensed to the number of poisoning events recorded. In 2005, Ontario retail pharmacies filled 5.3 million prescriptions of opioid analgesics and dispensed a total of 387.7 million doses of these medications. This implies a rate of approximately 1 ED contact per 62,000 doses, or per 840 prescriptions. This calculation necessarily excludes cases where no ED contact was made or where the overdose was identified as a 'complication of care', however, and also does not take into account use of over the counter codeine preparations or of certain opioids that appear to be uncommonly prescribed in Ontario, such as propoxyphene. Codeine and hydrocodone are included on grounds that, although these "weak" opioids are less toxic in overdose than stronger ones, their use has nonetheless been linked to ED contacts for poisoning at rates not substantially lower than those for other drugs (Dasgupta et al., 2006).

**Involvement of other substances**

Poisoning due to other medications and drugs was noted in 35% of incidents. Involvement of other substances is the norm in cases of fatal overdose, however. There are two likely explanations for this discrepancy. The first is that the detection ratio in ED settings may be considerably lower than in coroners' investigations: The latter may involve more thorough toxicological work, and investigators have

essentially unlimited access to the individual as well as, presumably, significantly less time pressure than is usual in emergency care. Moreover, it is possible that involvement of other drugs may sometimes go unrecorded in ED settings, or, at least, fail to be entered into administrative databases. The other probable explanation is simply that, as noted, certain drug combinations significantly increase the lethality of overdoses involving opioids. Such overdoses are thus likely to be overrepresented, perhaps dramatically so, in studies of fatalities, relative to the total set of overdoses occurring.

The most common other substances involved are benzodiazepines and acetaminophen. This is unsurprising. As noted, benzodiazepines are known to be a popular choice for combination with opioids among recreational users and have independent respiratory depressant effects. They are thus more likely to be used with opioids than other drugs, and this combination is, moreover, more likely to result in overdose necessitating emergency care. They also share common sources with prescription opioids: Physician prescriptions, pharmacies, and individuals who illicitly distribute prescription medications. People with access to prescription opioids may thus also have access to benzodiazepines.

Acetaminophen, by contrast, is not used recreationally. Although it is conceivable that it might be combined deliberately with opioids in some incidents of self-harm, the likeliest explanation for its appearance in ED records is that it is very frequently compounded with opioids in prescription medications. Acetaminophen is particularly

common in preparations including codeine (e.g., Tylenol 3) and oxycodone (e.g., Percocet), and its toxic effects may be risked, possibly unawares, by individuals taking these medications for the opioids they contain. The immediate effects of acetaminophen poisoning – typically nausea and vomiting – may also help decide overdose victims or others in favour of seeking emergency care, despite the fact that the much more serious hepatotoxic effects of the drug do not manifest for a period of two or three days (by which time overdoses on most opioids would have long resolved).

The fact that alcohol was recorded in only 3% of events probably does not reflect its actual level of involvement. The ICD-10 code recorded in these cases, "toxic effects of ethanol", may have been omitted in cases where alcohol toxicity was not judged to be clinically serious. Alcohol, however, may increase the risk of overdose, both directly, via its respiratory depressant effects, and indirectly via its impact on the absorption of some opioid preparations. It may be that ICD-10 poisoning codes are seldom used to indicate such effects.

Other recreational drugs represented included cocaine, which is not uncommonly mixed with opioids by users, and cannabis. The use of a poisoning code with cannabis is slightly curious given the limited toxicity of this drug. In all cases, however, it seems likely that the proportion of cases in which other substances were involved was somewhat higher than these data suggest, since the ICD-10 codes used

indicate "poisoning", and codes indicating mere intoxication were very rarely present in these data.

The third most common set of co-occurring substances were antidepressant and antipsychotic medications. Given the limited recreational potential of almost all drugs in these classes, these seem likeliest to occur in the context of intentional self-harm; access to these medications, for which there is no known, substantial illicit market, is itself likely to indicate the presence of psychiatric disorders that place sufferers at an increased risk of suicide. The relative prominence of tricyclic and tetracyclic antidepressants, which occur at half the rate of "other and unspecified antidepressants" despite being much less widely prescribed (Hemels et al., 2002), presumably reflects the much greater toxicity of these substances in overdose (e.g., Barbey & Roose, 1998).

**Demographic differences**

There were no significant gender differences in total rates of overdose on prescription opioids. Events of undetermined intent were more common among men, however, while self-harm was more common among women. The finding of gender parity in the overall rate is of some interest, since rates of substance misuse, abuse, dependence (e.g., Kessler et al., 2005), and overdose (e.g., Hall et al., 2008) are typically higher among men. This is not always the case in studies on opioids, however, which is suggestive of an intriguing gender difference in substance preference – particularly since the relative similarity of rates extends not only to prescription medications

(where there may be differences in access due to, for example, higher rates of physician contact by women), but also to heroin.

Age differences were substantial and highly significant. Total event rates were low among children under 15, and the majority of such events were coded as accidents. Self-harm was uncommon among people 65 or older, while those event types considered here as potentially due to intentional, non-medical use (accidents and events of undetermined intent) peaked among people aged 15 to 49. Among men, rates were noticeably higher among those 25 to 49 than among younger adults, while in women rates were very similar in these two age groups. The mean age of people presenting was somewhat younger among women, and this remained the case after incidents of self-harm were excluded.

**Prescription opioids and self-harm**

The study period saw large increases in accidental poisonings, but also substantial, though smaller, increases in the number of individuals using these medications in incidents of deliberate self-harm. Although most research has focused on "recreational" use and on overdoses presumed to result from such use, it therefore appears that increased availability of prescription opioids has also been associated with increased use of these drugs in suicide attempts or suicidal gestures. This is a comparatively little-studied phenomenon, perhaps in part because it is unclear whether access to opioids makes suicide attempts or other acts of self-harm more likely, or whether they simply displace other (possibly equally or more lethal) means.

Variation in the availability of lethal substances has, however, been linked to differences in rates of completed suicide: Easy access to pesticides, for example, is thought to underlie urban/rural differences in suicide mortality in many parts of the world (Gunnell et al., 2007). Although opioids are considerably less lethal in overdose, their availability may similarly influence rates of completed suicide or related harms, even in the absence of any change in rates of suicide attempt. In any case, if levels of ED contacts are a reasonable guide, self-harm comprises a considerable part of the clinical, and perhaps public health, burden of opioid misuse.

Existing investigations of opioid overdose have also generally ignored events arising in the course of care. Although such incidents could not be included in the present analysis, this is another substantial source of opioid-related harm that should be part of evaluations of the risks and benefits of these medications.

**Opioid poisoning and availability of specialist medical care**

The second part of the analysis presented considers the potential association between availability of specialist care, as measured by the number of specialist physicians per unit population in the local census division, and the rate of ED contacts for prescription opioid poisoning. As noted, such an association suggests itself because of the ways in which opioids are obtained. Sources of opioid analgesics are local, unlike those of most illicit drugs, and largely come, ultimately, from physician prescriptions. As there is some evidence that specialist providers are more likely to appropriately prescribe and manage these medications, their misuse may be more

common or more serious in areas where most care is provided by general practitioners.

Availability of specialist care was significantly associated with all outcomes. These associations were, however, non-linear. In all cases, the expected inverse association, such that a lower concentration of specialists was linked to higher event rates, was found in the lower parts of the distribution. After reaching minima at approximately 160 physicians per 100,000 population in all models, however, the predicted values begin to increase. The initial decrease can be interpreted as the expected effect, resulting from some combination of the proposed mechanisms: Poorer management of opioids; more inappropriate prescription of opioids; and an increased need for strong analgesics for conditions that might otherwise have been prevented or ameliorated.

The increase in events at higher concentrations of specialist providers is supported by the bivariate association (figure 2), which suggested such a relationship. One interesting interpretation of this finding is that greater availability of care leads to a greater general availability of opioids. Even if prescriptions written in specialist-rich areas are appropriate and medications well-managed, a much greater general availability of opioids may lead to more misuse. Although there are limited Canadian data in this area, work in the United States has uncovered large variations between states in the levels of opioid prescription, and, importantly, found an independent association between total opioids prescribed and the number of practicing surgeons

per unit population (Curtis et al., 2006). These geographical differences may be analogous to the changes noted over time in the United States (Paulozzi & Ryan, 2006; Dasgupta et al., 2006), where levels of prescriptions and rates of overdoses increased in step. Questions that follow concern the amounts of opioids prescribed in different areas within Ontario, whether they reflect overuse in some, under-use in others, or some combination of both, and whether some increase in non-medical use and in overdose is unavoidable when opioids are provided to all those who need them.

An alternative explanation, however, concerns unmeasured (and potentially unmeasurable) geographical differences. Toronto lies above the general trend of the first part of the curve of predicted values and includes some 20% of the provincial population. As a large urban area, it also has a high concentration of specialists, a high concentration of substance dependence treatment facilities, and some areas of significant poverty or social disorganization. A reanalysis of the data without Toronto, however, did not substantially alter the effect. It remains true, however, that the higher part of the distribution of the specialist availability variable includes relatively few regions, and that the improvement in model fit from the addition of a second transformation of the availability variable will have resulted from improved fit at these points. While intriguing, therefore, this result should be treated with caution. Analysis of data at a finer level of resolution might clarify the association.

The relationship between specialist care and poisoning events was markedly stronger for incidents of self-harm than for events of accidental or undetermined intent. While the latter outcome varies by a factor of approximately 1.5 across levels of specialist availability, self-harm varies by a factor of 3. This finding is somewhat unexpected. It is not entirely surprising that use of opioids in attempts at self-harm should follow a similar pattern to that of total poisonings, as this is another unintended use that might be expected to become more common where opioids are more readily available. What is surprising, however, is the relative strength of this association. One explanation concerns possible variations in overall background rates of self-harm. Specialist physicians tend to be concentrated in large cities (table 2), and these cities are also centres of psychiatric treatment. Evidence on urban/rural differences in completed suicide is decidedly mixed, however, with at least some North American studies (e.g., Singh & Siapush, 2002) reporting elevated incidence in rural areas. There are limited data on urban/rural differences in suicide attempts in Canada. Results from the 2002 Canadian Community Health Survey – cycle 1.2 show, however, that self-reported past-year suicide attempt is less common in Toronto (0.27%) than in the province as a whole (0.59%) and, notably, is most common in northern Ontario (1.25%), which has a very low levels of specialist availability (unpublished data). Bringing more detailed data to bear on this question would likely prove valuable.

**Model covariates**

Though included in all models as a conceptually important control variable, the availability of general medical care did not have a significant, independent association with any of the outcomes examined. This may be due in part to relatively limited variability in this indicator: The coefficient of variation at the census division level was 26%, as compared to 87% for specialist availability.

Most demographic variables were highly significant in all models, which indicates that the results obtained in the demographics-only model are not accounted for by differences in other factors. Rurality was non-significant in all models, and was also not significantly associated with poisoning rates at the bivariate level. This contrasts with work in parts of the United States, which has shown that overdose on prescription opioids is now somewhat more common in rural than in urban areas (CDC, 2005). It is unclear what underlies this difference. It is also not obvious, however, that such a difference should be expected to be universal; although rural areas throughout both countries have some potential risk factors in common, including low availability of medical care and often lower economic status, there are also substantial differences. Although there are regions of great poverty and deprivation in Ontario, particularly in remote areas, studies in the United States have included larger and more populous areas of rural poverty than exist in the province.

Median household income was inversely associated with overdose rates. Although interpretation of this effect is not straightforward due to the scale of the original

variable, the difference between 1SD below the mean and 1SD above the mean on this indicator corresponds to a difference in the total event rate of approximately 70% when other variables are held to their means. Income, wealth, education, and other measures of socioeconomic status are generally associated with better health at both the individual and regional levels.

The background rate of ED use for poisonings due to use of illicit substances or alcohol was highly significant in all models. The effect was fairly substantial; an increase in the rate of illicit drug or alcohol poisoning from 8 to 16 per 100,000 (corresponding to approximately -1SD to +1SD at the FSA level), for example, results in an increase in the rate of total opioid poisonings of 37% (from 8.6 to 11.8 per 100,000) when other variables are held to their means. This agrees with recent Canadian studies (e.g., Fischer et al., 2006) of people with a history of substance dependence, which have shown that use of prescription opioids is now very common in this population. More broadly, this association shows that prescription opioid misuse covaries with misuse of other substances. Along with the obvious similarities of the two phenomena, this suggests that they share common underlying causes. Although media reports, for example, sometimes suggest that most cases of opioid "addiction" are iatrogenic and represent a wholly different phenomenon than illicit drug dependence, the present results add to existing evidence indicating that prescription opioids, alcohol, and illicit drugs share a common appeal and a common demographic.

**Implications**

Results demonstrate that rates of poisoning from prescription opioid use increased substantially over the study period, and that the rate of this increase was relatively steady. Although rates since the end of the study period are unknown, it is clear that ongoing monitoring of this issue is crucial. Unlike the United States, which operates an ED-based system that centralizes records of drug-related harms (the Drug Abuse Warning Network), Canada does not systematically monitor such events. Such a system would have important advantages. In addition to rapid identification of emerging clusters of drug overdose (of the kind that might appear as the result of increases in illicit drug purity or availability), tracking of ED contacts would make it possible to react more expeditiously to broader trends in poisonings or other events (Kleine et al., 2007).

What the policy reaction to increased rates of opioid overdose should be, however, is not obvious. Opioids are a class of drugs which, like sedative/hypnotics such as the benzodiazepines and stimulants such as methylphenidate, have important medical uses but also significant potential for misuse. Significant efforts have been made to ensure access to opioids, and the expansion of their use may represent an important advance in the relief of pain and the treatment of opioid dependence. The risk of overdose per unit consumed is also relatively small. Finally, it is also not always clear what overall impact changes in the use of individual substances or classes of substance have, from a public health perspective, on the level of substance-related harms in general. For existing users, some substances are highly substitutable, as in

the case of heroin and the opioid analgesics themselves. The OSDUHS survey has also found decreases, often sharp, in the use of various substances among Ontario adolescents over the past 10 years. It is intriguing that these declines have coincided with a period of increased availability and misuse of the opioid analgesics.

These considerations make policy approaches to the increasing misuse of opioids particularly fraught. Broad attempts to limit their use may negatively affect people for whom they are necessary and appropriate medications. Even efforts to improve oversight of prescribers might discourage physicians from providing opioids in cases where they would be appropriate. One obvious approach is to improve medical education with respect to the management of pain; as noted, many general practitioners do not feel adequately prepared for the management of patients requiring strong opioids (Hutchinson et al., 2006). Another possibility concerns the monitoring of prescription patterns. Such data have been put to use in pharmaceutical companies' marketing efforts in the United States (Van Zee, 2009). A better use might involve the identification of opportunities to intervene – educationally rather than punitively, in most cases – in situations where physicians appear to be prescribing excessively or indiscriminately. It is not clear, however, that identifying the small proportion of physicians with obviously problematic prescribing practices would have an enormous impact on opioid availability, and such monitoring might be unpopular with physicians in any case.

A further possibility concerns the use of "opioid contracts", which are agreements (often not actually identified as "contracts") between providers and patients that explicitly set out the conditions for treatment with opioid analgesics. These almost invariably include prohibitions on selling or distributing medication, using excessive amounts, and seeking other sources of prescriptions (Fishman, 1999). Such documents are sometimes intended to be principally educational (Gitlin, 1999), however, and it is not clear how effective they are in deterring these behaviours. In any case, physicians, medical professional organizations, and medical educators probably have the greatest ability to reduce or ameliorate the consequences of opioid misuse without adversely affecting care.

The future of opioid prescription misuse is unclear, other than the obvious fact that it can be expected to persist. In the modern era, misuse of opioids has waxed and waned with variations in regulation, availability, and with cultural shifts generally. More novel substances such as synthetic sedative-hypnotics and stimulants have had similar histories. Illicit use of some specific drugs and classes of drugs, such as methaqualone and the barbiturates, has almost ceased, but only because they have been withdrawn from sale or displaced by other medications. Use of medical opioids cannot be eliminated, and it remains to be seen how effective policy approaches will be in reducing levels of misuse and related consequences, such as overdose.

**Limitations**

The analysis presented has several important limitations. First, as noted, the analysis is an ecological one: Data are aggregated to regions, but inferences are drawn about outcomes for individuals. Although the large number of areas analyzed may have mitigated this problem, this study remains vulnerable in principle to the difficulties common to ecological analyses.

The nature of the geographical data available was also unfortunate, in that the primary units of analysis, FSAs, did not nest within the larger regions (census divisions) for which physician availability data were obtainable. This necessitated the estimation of values for a substantial proportion of data by using a weighted average of regional values. Although this approach arguably does not necessarily result in less accurate results than assigning census division values to those FSAs that fully nest within them, it highlights the somewhat coarse and approximate nature of the exposure measure. One assumption that may be problematic is that census district level indicators accurately reflect availability of services. Although it is likely that census divisions are sufficiently large that this is not a critical issue, these census boundaries are partly arbitrary, and use of care in an adjacent region may be common. This may be a particular issue in the case of areas bordering on Toronto or Ottawa, which have very high concentrations of specialists; apparent relative scarcities in the suburbs of these cities may actually reflect the ease of travel to care in a nearby city. Any bias of this type should, however, be conservative.

An equally important issue concerns the possibility of confounding by unmeasured variables. This analysis involves geographical differences, and attempts to take into account population differences in age and sex distributions, income, illicit drug and alcohol poisoning, rurality, and availability of general practitioners. These are clearly not the only potential determinants of prescription opioid poisoning rates, however. Like other behaviours or health outcomes, much spatial variation in rates of problematic substance use is not easily accounted for by measured variables. Some variation may be simply "cultural" and nearly unmeasurable. One potential difficulty is that the number of recorded contacts reflects not only of the background incidence of opioid overdose, but also the likelihood that such an event will result in an ED visit. In the case of relatively mild poisonings, such differences might be substantial, being driven in part, perhaps, by proximity to emergency care. Proximity to an ED is itself likely to be correlated with specialist availability. This association may result in a conservative bias, however, as it suggests that people in areas with low availability of specialists may also be less likely to visit an ED, as a result of poorer access. The inclusion of an indicator of ED use for other drug poisonings is very important with respect to this type of unmeasured geographical difference, as this is another outcome that can be expected to vary with such things as availability of EDs and propensity to seek care.

Although this project is concerned with poisoning from prescription opioids, it is not always possible to distinguish prescription from illicit drugs. Since heroin is metabolized to morphine in the body, determination of the substance responsible for

overdose will sometimes be impossible, or will rely on patient information, the detection of adulterants commonly found in heroin, or other indications that lead to a strong presumption of heroin use. Records are heroin use are sparse in these data, however, with a total of 236 cases recorded across the study period. Since it is likely that clinicians would have information sufficient to distinguish between heroin and prescription opioid use in many cases, it seems unlikely that confusion of this kind had a significant impact on the results. This study also includes all contacts for which opioid poisoning is listed as a diagnosis. It therefore includes cases in which other drugs or other conditions contribute to the admission.

It is also important to note that the data in this study reflect only ED visits for opioid poisoning. They do not include incidents of overdose for which no help was sought, which were dealt with by physicians in other contexts (e.g., in institutional settings), or fatal poisonings for which no ED contact occurred. Incidences and numbers of events presented here therefore represent a subset of all those poisonings that occurred in the province within the study period.

The available data on ED visits are also limited in several ways. ICD codes for diagnosis do not, in general, make it possible to distinguish different prescription opioids. A more serious limitation is the nature of the information available on types of events. Although I have followed existing work in including 'accidental' overdoses and 'events of undetermined intent' in the final model, it is important to note that not all of these incidents will have been the result of deliberate misuse of

opioids for recreational purposes. Instead, these two broad categories include several other possibilities, notably attempts at self-harm which could not be firmly identified as such and accidental overdoses resulting from genuine errors in dosing on the part of patients or providers.

**Conclusion**

This study sought to describe the epidemiology of prescription opioid overdose in Ontario, as measured by emergency department contacts, and to explore the association between this outcome and the availability of specialist care. Results demonstrate that total contacts for opioid poisoning rose steadily across the study period, and that regional variation in rates is associated with the local concentration of specialist physicians.

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Zador D, Sunjic S, Darke S. Heroin-related deaths in New South Wales, 1992: toxicological findings and circumstances. Med J Austr 1996; 164:204.

**Date:** Thu, 21 May 2009 10:30:56 -0400 [21/05/09 10:30:56 AM EDT]
**From:** Research Ethics Board <reb@brocku.ca>
**To:** Terrance Wade <twade@brocku.ca>, "'sv07ed@brocku.ca'" <sv07ed@badger.ac.brocku.ca>
**Cc:** 'Michelle McGinn' <rebchair@brocku.ca>
**Subject:** REB 08-332 - Accepted as is with note

DATE: May 21, 2009

FROM: Michelle McGinn, Chair
Research Ethics Board (REB)

TO: Terrance Wade, Community Health Sciences
Scott Veldhuizen

FILE: 08-332 WADE/VELDHUIZEN
Masters Thesis/Project

TITLE: Opioid poisoning and access to specialized medical care in Ontario, 2002-2006

The Brock University Research Ethics Board has reviewed the above research proposal.

**DECISION: ACCEPTED AS IS WITH NOTE**

**Please note:**

**To complete your file, please forward a copy of the documentation from CIHI and CAMH providing you with access to data.**

This project has received ethics clearance for the period of **May 21, 2009 to May 30, 2010** subject to full REB ratification at the Research Ethics Board's next scheduled meeting. The clearance period may be extended upon request. ***The study may now proceed.***

Please note that the Research Ethics Board (REB) requires that you adhere to the protocol as last reviewed and cleared by the REB. During the course of research no deviations from, or changes to, the protocol, recruitment, or consent form may be initiated without prior written clearance from the REB. The Board must provide clearance for any modifications before they can be implemented. If you wish to modify your research project, please refer to http://www.brocku.ca/researchservices/forms to complete the appropriate form Revision or Modification to an Ongoing Application.

Adverse or unexpected events must be reported to the REB as soon as possible with an indication of how these events affect, in the view of the Principal Investigator, the safety of the participants and the continuation of the protocol.

If research participants are in the care of a health facility, at a school, or other institution or community organization, it is the responsibility of the Principal Investigator to ensure that the ethical guidelines and clearance of those facilities or institutions are obtained and filed with the REB prior to the initiation of any research protocols.

The Tri-Council Policy Statement requires that ongoing research be monitored. A Final Report is required for all projects upon completion of the project. Researchers with projects lasting more than one year are required to submit a Continuing Review Report annually. The Office of Research Services will contact you when this form *Continuing Review/Final Report* is required.

Please quote your REB file number on all future correspondence.

MM/an

Research Ethics Office

Brock Research, MC D250A-1

Brock University

500 Glenridge Avenue, St. Catharines, ON L2S 3A1

Phone 905-688-5550 ext. 3035

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http://www.brocku.ca/researchservices/Ethics_Safety/Humans/Index.php

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July 3, 2009

Social, Prevention, and Health Policy Research
Center for Addiction and Mental Health
33 Russell Street
Toronto ON M5S 2S1

Attention: Russell Callaghan
Scott Veldhuizen

Dear Russell:

I am writing to inform you that CIHI has approved your request to allow Scott Veldhuizen and yourself to access and use NACRS data from fiscal year 2002-03 through 2005-06 originally provided to you on December 10, 2007 for your project "The comparative impact and clinical correlates of methamphetamine use in Canada: An examination of hospital-admission records from the Discharge Abstract Database, 1996-2005". CIHI's expectation is that Mr. Veldhuizen will use these data only for purposes relating to his project "Opioid poisoning and access to specialized medical care in Ontario, 2002-2006".

As communicated when these data were originally released, it remains CIHI's understanding that the only copy made of the contents of the original CD are stored on the hard drive of a single non-network computer in your office at the Centre for Addiction and Mental Health. Further, it is our understanding that you remain the sole possessor of the password to access the data, and that Mr. Veldhuizen will make requests on an as-needed basis to be granted access the data on your computer.

The data will continue to be kept only for the time period specified in section 14 of the *Non-Disclosure/Confidentiality Agreement* that you signed as part of your original request for record-level data. It will be your responsibility to ensure that the data file, including all whole and/or partial copies are destroyed by no later than November 2012.

When your retention period is nearing its end, please be sure that you contact CIHI for instructions on how to proceed to securely destroy the data. At that time, CIHI will expect that the original CD will still be in your possession, and that you have kept track of all copies that have ever been made of the original data. All whole and/or partial copies of the data reproduced, located, stored or found on servers,

hard drives, CDs/ DVDs, USB keys, laptops, paper, and any other format, device or media regardless of location, will need to be duly and securely destroyed such that reconstruction is not reasonably foreseeable.

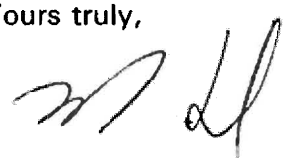
I encourage both Mr. Veldhuizen and yourself to take this opportunity to familiarize yourselves with the updated Non-Disclosure/Confidentiality Agreement that you have signed as part of your request to have the originally released data approved for this alternate purpose/project.

Also, please be reminded that prior to publishing, reporting or otherwise disclosing material, you must aggregate information to avoid residual disclosure of the identity of individuals or institutions by ensuring that each cell has at least five observations, unless express written authorization is provided by CIHI.

If you wish to review data quality information about the source databases, please refer to the CIHI website, in the section pertaining to data quality.
http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=quality_e

If you have any questions, please do not hesitate to call me.

Yours truly,



Marcus Loreti
Program Lead, Decision Support Services
Canadian Institute for Health Information
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Toronto, Ontario M2P 2B7
☎-416-481-1616 x5408
snap@cihi.ca

# CURRICULUM VITAE

Scott Veldhuizen
MA Candidate
Brock University
February, 2010

## I. Personal Information

| | |
|---|---|
| Citizenship | Canadian |

## II. Education

| | |
|---|---|
| M.A. (candidate) | Community Health, Brock University, 2007-present. |
| B.A. | Economics and Classical Civilization, University of Toronto, 1996-2000. |
| | University of Windsor, 1994-1996. |

## III. Awards

| | |
|---|---|
| 2008 | Brock University Excellence in Research Award. |

## IV. Research position

| | |
|---|---|
| 2003-present | Research Analyst, Health Systems Research and Consulting Unit, Centre for Addiction and Mental Health. |

## V. Other positions

| | |
|---|---|
| 2001-2002 | Senior systems developer, CIBC Mortgages, Inc. (contract) |
| 2000 | Developer, Ontario Ministry of Health and Long-Term Care (contract) |
| 1999-2000 | Developer, Environment Canada (contract) |
| 1999 | Developer, Ryder Integrated Logistics (contract) |
| 1999 | Developer, Gemcom Software (freelance) |
| 1998 | Developer, Reuters Canada (freelance) |
| 1997-1998 | Developer, Canadian Centre for Philanthropy (freelance) |
| 1996-1999 | Developer, Noranda Mining and Exploration (freelance) |

## VI. Research Awards

1. Collaborator with Dr. Ayal Schaffer (PI), Dr. Amy Cheung, Dr John Cairney, Dr Paul Kurdyak, Dr. Anthony Levitt. An Epidemiological Comparison of Bipolar

Disorder and Major Depressive Disorder: Implications for Improving Diagnosis and Management ($73,250 funded by Canadian Institutes for Health Research), March 2008-February 2010.

## VII. Scientific Peer Review Activities

| | |
|---|---|
| 2009 | *European Psychiatry* |
| 2008-2009 | *American Journal of Epidemiology* |
| 2008 | *International Journal of Health Geographics* |
| 2008-2009 | *Journal of Gambling Issues* |
| 2008 | *Drug and Alcohol Dependence* |

## VIII. Publications

Refereed journal articles

1. Schaffer A, Cairney J, **Veldhuizen S**, Kurdyak P, Cheung AH, Levitt A. A Population-Based Analysis of Distinguishers of Bipolar Disorder from Major Depressive Disorder. Journal of Affective Disorders (in press).

2. Brennan DJ, Ross, LE, Dobinson C, **Veldhuizen S**, Steele L. Men's sexual orientation and health in Canada. *Canadian Journal of Public Health* (in press).

3. Cairney J, **Veldhuizen S**, Faulkner G, Schaffer A, Rodriguez C. Bipolar Disorder and Leisure-Time Physical Activity: Results from a National Survey of Canadians. *Mental Health and Physical Activity* 2009;2:65-70.

4. Cairney J, Hay JA, **Veldhuizen S**, Missiuna C, Faught BE. Developmental coordination disorder, gender and the activity deficit over time: A longitudinal analysis of participation trajectories in children with and without coordination difficulties. *Developmental Medicine & Child Neurology* (in press).

5. Steele LS, Ross LE, Dobinson C, **Veldhuizen S**, Tinmouth J. Women's sexual orientation and health: Results from a Canadian population-based survey. *Women & Health* (in press).

6. Callaghan RC, **Veldhuizen S**, Leatherdale S, Murnaghan D, Manske S. Contraband cigarette use among adolescent daily smokers in Canada. *Canadian Medical Association Journal* (research letter) (in press).

7. Cheung A, Dewa C, Cairney J, **Veldhuizen S**, Schaffer A. Factors Associated with Use of Mental Health Services for Depressed and/or Suicidal Youth Aged 15-24. *Community Mental Health Journal* 2009:28 (ePub).

8. Schaffer A, Cairney J, Cheung AH, **Veldhuizen S**, Kurdyak P, Levitt A. Prevalence and Treatment for Bipolar Disorder Among Immigrants: Results from an Epidemiological Survey. *Canadian Journal of Psychiatry* 2009;54(11):734-742.

9. Bassani DG, Padoin CV, Philipp D, **Veldhuizen S**. Estimating the number of children exposed to parental psychiatric disorders through a national health survey. *Child and Adolescent Psychiatry and Mental Health* (in press).

10. Cairney J, Hay J, **Veldhuizen S**, Missiuna C, Faught BE. Comparing probable case-identification of Developmental Coordination Disorder using the short form of the Bruininks-Oseretsky Test of Motor Proficiency and the Movement ABC. *Child: Care, Health & Development* (in press).

11. **Veldhuizen S**, Wade TJ, Cairney J. Patterns of alcohol consumption among Canadians taking benzodiazepines and related drugs. *Pharmacoepidemiology and drug safety* (in press; published online, December 30, 2008); doi:10.1002/pds.1702.

12. Bassani DG, Padoin CV, **Veldhuizen S**. Counting children at risk: Exploring a method to estimate the number of children exposed to parental mental illness using adult health survey data. *Social Psychiatry and Psychiatric Epidemiology* (in press; published online, June 23, 2008).

13. Cairney J, Missiuna C, **Veldhuizen S**, Wilson B. Evaluation of the psychometric properties of the Developmental Coordination Disorder Questionnaire for parents (DCD-Q): Results from a community based study of school-aged children. *Human Movement Sciences* 2008;27:932-940.

14. Cairney J, Wade TJ, Faulkner G, **Veldhuizen S**. Changes over time in Physical Activity and Psychological Distress among Older Adults. *Canadian Journal of Psychiatry* (in press).

15. Cairney J, Schmidt LA, **Veldhuizen S**, Kurdyak P, Hay J, Faught BE. Left-handedness and developmental coordination disorder. *Canadian Journal of Psychiatry* (in press).

16. Faught BR, Cairney J, Hay J, **Veldhuizen S**, Missiuna C, Spironello CA. Screening for Motor Coordination Challenges in Children using Teacher Ratings of Physical Ability and Activity. *Human Movement Sciences* (in press).

17. Cairney J, Corna L, **Veldhuizen S**, Herrmann N, Streiner DL. Co-morbid Depression and Anxiety in Later Life: Patterns of Association, Illness Severity and Impairment. *American Journal of Geriatric Psychiatry* (in press).

18. de Ruiter WK, Faulkner G, Cairney J, **Veldhuizen S**. Physical activity, smoking and harm reduction: Who are the physically active smokers? *American Journal of Public Health* (in press).

19. Cairney J, Corna LM, **Veldhuizen S**, Kurdyak P, Streiner DL. The Social Epidemiology of Affective and Anxiety Disorders in Later Life. *Canadian Journal of Psychiatry*, Canadian Journal of Psychiatry 2008;53(2):104–111.

20. Strike C, Wenghofer E, Gnam W, Hillier W, **Veldhuizen S**, Millson M. Clinical practice guideline adherence with peer assessment: The case of methadone maintenance treatment. *Journal of Continuing Education in the Health Professions,* 2007;27(4):208–213.

21. Schaffer A, Cairney J, **Veldhuizen S**, Cheung A, Levitt A. Antidepressant use in a community sample of bipolar and major depressive disorder subjects with or without comorbid anxiety. *Journal of Clinical Psychiatry*, 2007;68;11:1785-1792.

22. Cairney J, **Veldhuizen S**, Kurdyak P, Missiuna C, Faught BE, Hay J. Evaluating the CSAPPA sub-scales as potential screening instruments for Developmental Coordination Disorder. *Archives of Disease in Childhood*; 2007;92:987-991.

23. Callaghan RC, Tavares J, Taylor L, **Veldhuizen S.** A national survey of primary methamphetamine-related admissions to adolescent residential substance-abuse treatment facilities in Canada, 2005-2006. *Canadian Journal of Psychiatry*, 2007 2007;52(10).

24. Corna LM, Cairney J, **Veldhuizen S**, Streiner DL, McCabe L, Herrmann N. Panic disorder in later life: Results from a large, national survey of Canadians. *International Journal of Psychogeriatrics*; 2007;19(6):1084-96.

25. **Veldhuizen S**, Urbanoski K, Cairney J. Geographical variation in the prevalence of substance-related problems in Canada. *Canadian Journal of Psychiatry*, 2007; 52(7):426-433.

26. Rush BR, **Veldhuizen S**, Adlaf E. Mapping the prevalence of problem gambling and its association with treatment accessibility and proximity to gambling venues. *Journal of Gambling Issues*, 2007;20.

27. **Veldhuizen S**, Cairney J, Kurdyak P, Streiner DL. On the sensitivity of the K6 as a screen for disorder in community mental health surveys: A cautionary note. *Canadian Journal of Psychiatry*, 2007; 52: 256–259.

28. Cairney J, **Veldhuizen S**, Wade TJ, Kurdyak P, Streiner DL. Evaluation of Two Measures of Psychological Distress as Screeners for Current Depression in the General Population. *Canadian Journal of Psychiatry,* 2007;52:111–120.

29. Cairney J, McCabe L, **Veldhuizen S**, Corna L, Streiner DL, Herrmann N. Epidemiology of Social Phobia in Later Life. *American Journal of Geriatric Psychiatry*, 2007;15:224-233.

30. Cairney J, Pevalin DJ, Wade TJ, **Veldhuizen S**, Arboleda-Florez J. 12-month psychiatric disorder among single mothers: The role of marital history. *Canadian Journal of Psychiatry*, 2006;51:671–676.

31. McCabe L, Cairney J, **Veldhuizen S**, Streiner DL, Herrmann N. Prevalence and Correlates of Agoraphobia in Older Adults. *American Journal of Geriatric Psychiatry,* 14:515-522, June 2006.

32. Schaffer A, Cairney J, Cheung AH, **Veldhuizen S**, Levitt AJ. Use of Treatment Services and Pharmacotherapy for Bipolar Disorder in a General Population-Based Mental Health Survey. *Journal of Clinical Psychiatry,* 2006;67:386-393.

33. Streiner DL, Cairney J, **Veldhuizen S**. The Epidemiology of Psychological Problems in the Elderly. *Canadian Journal of Psychiatry,* 2006;51(3):185-191.

34. Schaffer A, Cairney J, Cheung AH, **Veldhuizen S**, Levitt A. Community Survey of Bipolar Disorder in Canada: Lifetime Prevalence and Gender Differences. *Canadian Journal of Psychiatry,* 2006;51(1):9-16.

Book chapters

1. **Veldhuizen S**, Cairney J, Streiner DL (2009). The RDC Archipelago. In Streiner, DL & Sidani, S (Eds.), *When Research Goes Off the Rails*. New York: Guilford Press.

2. Cairney J, **Veldhuizen S**, Wade TJ (in press). Intersecting social statuses and psychiatric disorder: New conceptual directions in the social epidemiology of mental disorder. In DL Streiner and J Cairney (Eds.), *Psychiatric Epidemiology in Canada.*

3. Hay J, **Veldhuizen S**, Cairney J. (2008). Tracking the relationship between motor proficiency and BMI over a 24-month period among Canadian school children. Pp. 129-133 in Toivo Jürimäe, Neil Armstrong and Jaak Jürimäe (Eds.) Children and Exercise XXIV: The proceedings of the 24th pediatric work physiology meeting. London UK: Routledge.

Refereed conference posters

1. **Veldhuizen S**, Callaghan RC, Wade T. "Opioid analgesic overdose in Ontario, 2002 to 2006". Canadian Academy of Psychiatric Epidemiology 2009 conference, St. John's, NL, August 27, 2009.

2. **Veldhuizen S**, Missiuna C, Cairney J, Pollock N, Cousins M. "Performance on specific motor tasks in children with DCD with or without comorbid ADHD". DCD VIII, Baltimore, Maryland, June 23-26, 2009.

3. Cairney J, Missiuna C, Pollock N, Cousins M, Schmidt L, Russell D, Macdonald K, **Veldhuizen S**. "Description of motor, attention, and intellectual characteristics in a population-based sample of children screened for motor impairment". DCD VIII, Baltimore, Maryland, June 23-26, 2009.

4. Schaffer A, Cairney J, **Veldhuizen S**, Cheung A, Kurdyak P, Levitt A. "A population-based comparison of suicidality among bipolar disorder and major depressive disorder subjects". American Psychiatric Association 2009 conference, San Francisco, CA, May 16-21, 2009.

5. **Veldhuizen S**, Cairney J, Wade TJ. "Effects of reporting period on the epidemiology of major depression". Canadian Academy of Psychiatric Epidemiology 2008 conference, Vancouver, BC, September 4, 2008.

6. **Veldhuizen S**, Cairney J, Wade TJ. "Age-related variation in the chronicity and severity of major depression". 33rd Annual Harvey Stancer Research Day, Department of Psychiatry, University of Toronto, Toronto, ON, June 19, 2008.

7. Rush BR, Castel S, Brands B, Toneatto T, **Veldhuizen S**. "Validation and comparison of screening tools for mental disorders in substance abusers". College on Problems of Drug Dependence 70th Annual Meeting, San Juan, Puerto Rico, June 14-19, 2008.

8. **Veldhuizen S**, Wade TJ, Cairney J. "Patterns of alcohol consumption among Canadians taking benzodiazepines and related drugs". Canadian Academy of Psychiatric Epidemiology 2007 conference, Montreal, QC, November 15th, 2007.

9. Cairney J, **Veldhuizen S**, Hay JA, Faught BE. "The utility of brief teacher ratings in the identification of developmental coordination disorder". American Psychiatric Association 2007 conference. San Diego, CA, May 23, 2007.

10. **Veldhuizen S**, Urbanoski K, Rush BR. "Alcohol consumption and alcohol dependence in the presence of psychiatric disorder". Canadian Academy of Psychiatric Epidemiology 2006 conference. Toronto, ON, November 9th, 2006.

11. Schaffer A, Cairney J, **Veldhuizen S**. "Antidepressant Use in a Community Sample of Bipolar and Unipolar Subjects: Effect of Diagnosis and Comorbid Anxiety". 2nd Biennial Conference of the International Society for Bipolar Disorders. Edinburgh, Scotland, August 2-4, 2006.

12. **Veldhuizen S**. "A severity adjustment for estimates of unmet need for depression treatment". 32nd Annual Harvey Stancer Research Day, Department of Psychiatry, University of Toronto, Toronto, ON, June 15th, 2006.

13. Corna LM, Cairney J, **Veldhuizen S**, Streiner DL, McCabe L. "The epidemiology of panic disorder in later life: Results from a large, national survey of Canadians". American Psychiatric Association 2006 Conference, Toronto, ON, May 25, 2006.

14. Cairney J, **Veldhuizen S**, Corna LM, Streiner DL, McCabe, L, Herrmann, N. "Co-morbid Depression and Anxiety in Later Life: Patterns of Associations and Impairment". American Psychiatric Association 2006 Conference, Toronto, ON, May 25, 2006.

15. **Veldhuizen S**, Cairney J, Urbanoski K, Rush BR. "Geographical variation in risk for substance use disorders in Canada". Canadian Academy of Psychiatric Epidemiology 2005 conference, Vancouver, BC, November 3rd, 2005.

16. Rush BR, Bassani D, Urbanoski K, Wild C, Strike C, Castel S, Somers J, Kimberley D, **Veldhuizen S**. "Prevalence of co-morbidity among addictive disorders and other mental disorders in the Canadian Population". Canadian Psychiatric Association 55th annual conference, Vancouver, BC, November 3-6, 2005.

17. Rush BR, **Veldhuizen S**, Adlaf E. "Environmental risk factors for problem gambling in Ontario." Canadian Public Health Association, 96th annual conference, Ottawa, ON, September 20th, 2005.

18. **Veldhuizen S**, Rush BR. "Substance use and symptom profiles in chronic and severe mental illness: Alcohol, cannabis, and cocaine." 31st Annual Harvey Stancer Research Day, Department of Psychiatry, University of Toronto, Toronto, ON, June 16th, 2005.

19. Urbanoski K., Rush BR, **Veldhuizen S**, Aubry T, Durbin J. "Treatment outcome in community mental health consumers with concurrent substance use disorders". 27th Annual Scientific Meeting of the Research Society on Alcoholism, Vancouver BC, June 26-30, 2004.

Conference presentations

1. Cairney J, **Veldhuizen S**. "'Unmet' need for mental health services: What can epidemiological surveys tell us?" Invited presentation at the International Symposium of Needs Assessment and Needs-based Planning for Substance Use Services and Supports, Toronto, Ontario, Canada, June 9th, 2008.

2. Cairney J, **Veldhuizen S**, Corna L, Wade TJ, Streiner DL. "Further Considerations on the Association between Age and Depression: Results from the Canadian Community Health Survey (1.2)." Canadian Association on Gerontology Annual Meeting, Quebec City, QC, October 27th, 2006.

3. Streiner, DL, Corna, L, **Veldhuizen, S**, Cairney, J. Canadian Academy of Psychiatric Epidemiology 2005 conference, Vancounver, BC. "Anglophone and Francophone rates of depression: Cultural or language differences?" Canadian Academy of Psychiatric Epidemiology 2005 conference, Vancounver, BC, November 3, 2005.

4. Cairney, J, Streiner, DL, **Veldhuizen, S**, Corna, L, McCabe, L. "12–month and Lifetime Prevalence of Social Phobia in Later Life: Risk Factors and Co-morbidity". Canadian Academy of Psychiatric Epidemiology 2005 conference, Vancounver, BC, November 3, 2005.

5. Schaffer A, **Cairney J**, Cheung A, Veldhuizen S, Levitt A. "Gender Differences in Service Utilization and Treatment for Bipolar Disorder." Presented as part of symposium on International Comparison of Service Utilization for Mood Disorders. 57th Institute on Psychiatric Services, American Psychiatric Association, San Diego, United States, October 6th, 2005.

6. McCabe L, Cairney J, **Velduizen S**, Herrman N, Streiner DL. "Agoraphobia in the Elderly: Results from a National Probability Sample." Harvey Stancer Research Day, Department of Psychiatry, University of Toronto, Toronto, Ontario, June 16, 2005.

7. McCabe L, Cairney J, **Veldhuizen S**, Hay J, Faught BE. "Correlates of Exercise as a Coping Strategy for Stress: Results from a National Survey of Canadians." American College of Sports Medicine, 52nd Annual Meeting, Nashville, Tennessee, USA, June 2nd, 2005.

8. Urbanoski, K, Rush, B, **Veldhuizen, S**, Aubry, T, & Durbin, J. "Treatment outcome in community mental health consumers with concurrent substance use disorders." 27th Annual Scientific Meeting of the Research Society on Alcoholism, Vancouver BC, June 26-30, 2004.

Published Abstracts

1. **Veldhuizen S**, Cairney J, Hay JA, Missiuna C, Faught BE (2007). Fitness and fatness in children: examining risk over time in a large cohort of school-aged children. Acta Kinesiologiae Universitatis Tartuensis 12(Suppl.): 200-201.

2. Hay JA, Cairney J, **Veldhuizen S**, Missiuna C, Faught BE (2007). Tracking waist girth and BMI in children: the contribution of motor proficiency to overweight and obesity. Acta Kinesiologiae Universitatis Tartuensis 12(Suppl.): 99-100.

3. Cairney J, **Veldhuizen S**, Hay JA, Missiuna C, Faught BE (2007). Motor proficiency, aging and participation in physical activities: is there an activity deficit over time? Acta Kinesiologiae Universitatis Tartuensis 12(Suppl.): 62-63.

4. Schaffer A, Cairney J, **Veldhuizen S** (2006). Antidepressant use in a community sample of bipolar and unipolar subjects: Effect of diagnosis and comorbid anxiety. Bipolar Disorders (8) Suppl: 37.

5. McCabe L, Cairney J, **Veldhuizen S**, Hay J, Faught BE (2005). Correlates of Exercise as a Coping Strategy for Stress: Results from a National Probability Survey of Canadians. Medicine and Science in Sports and Exercise, 37(5) Suppl: S175.

Reports

1. Lin E, **Veldhuizen S,** Goering P. Feasibility of policy-oriented research on depression with linked administrative and survey data. Toronto, ON: Centre for Addiction and Mental Health, 2006.

2. Rush BR, **Veldhuizen S**, Adlaf E, Corea L, Vincent S. Assessing the geo-spatial association in Ontario between the prevalence of problem gambling, treatment availability, and help-seeking. Toronto, ON: Centre for Addiction and Mental Health, 2005.

3. Rush BR, Zaslavska N, **Veldhuizen S**. A comparison of alternative approaches for screening for substance abuse in two community mental health services. Toronto, ON: Centre for Addiction and Mental Health, 2005.